The Journal of
Nervous and Mental Disease

Vol. 125, No. 1 JANUARY—MARCH 1957 Serial No. 901

THE DETECTION OF SCHIZOPHRENIA IN INFANCY
A Preliminary Report[1,2]

BARBARA FISH M.D.[3]

I. Introduction

In recent years workers in childhood schizophrenia have shifted their attention from the description of its psychopathology to investigations of etiology and genesis. While it is known that schizophrenic children, like all other children, (and frequently more dramatically than most) are unquestionably molded by dynamic interaction with their families and the culture as a whole, the opinion is growing that we will not unlock the riddle of schizophrenia until we learn more about the underlying constitutional factors. Research in this area would undoubtedly be advanced if it were possible to detect schizophrenia or its antecedents early in life, and study the developing manifestations by direct observation. The following investigation was predicated upon the belief that Bender's conceptions of childhood schizophrenia provide the key to such early diagnosis. It was planned as a pilot study to see whether one could examine a random population in the light of Bender's criteria, and so detect infants who would later become schizophrenic.

Over the past 20 years Bender has delineated the clinical features of childhood schizophrenia (4, 5) and has summarized the data on some 850 children so diagnosed. "The diagnosis has been confirmed in late adolescence or adulthood in 89% of the earliest 250 cases." (10).

Bender demonstrated that characteristic deviations from normal development are present in the histories of schizophrenic children, often at birth (5, 7, 8). In 1950 she added a new perspective through the recognition that the patterning of schizophrenic children may be understood from the resemblance to features of the fetal infant as described by Gesell (26). The similarities include 1) homeostatic instability, seen in poor temperature control, vasomotor instability, allergic phenomena, and respiratory and gastrointestinal difficulties; 2) fluctuation in and out of a torporous state of consciousness with disturbed, unpatterned sleep; 3) immature, molluscous muscle tone; 4) infantile posture and motor activity, based upon persistent tonic neck reflexes; 5) patterning dominated by an over-all plasticity,* similar to the embryo's "many potentialities of development both in quality, direction and speed." Thus, "the pattern of growth is characterized by retardation and precocity, alternately and simultaneously. . . . From these considerations the concept has grown that childhood schizophrenia represents a lag in maturation within the embryological level of development in all the areas that are the prerequisite of future behaviors in all fields—motor, adaptive, language and personal-social." (8). A preliminary statistical study confirmed a high degree of specificity for the pathognomonic features which gave rise to this hypothesis (9).

Bender considers that anxiety in schizophrenic children and difficulty in identifying

[1] This study was initiated at Bellevue Hospital, New York, and is now being continued at New York Hospital-Cornell Medical Center, New York.

[2] Part of this study was carried out during the tenure of a Fellowship of the National Foundation for Infantile Paralysis.

[3] From the Departments of Pediatrics and Psychiatry, The New York Hospital-Cornell University Medical College, New York

themselves to their own body are secondary to the primary physiological immaturity, and in turn give rise to difficulties in identifications and relationships with others and the varied spectrum of psychopathology which follows (7, 8). According to this view, although the psychological manifestations vary with age, physiological crises, and environmental vicissitudes; the fundamental biologic symptomatology remains. Bender demonstrated this in a 30 to 40-year follow-up on 90 adult schizophrenic patients (11). However, schizophrenia as thus defined is not synonymous with psychosis although the schizophrenic children "retain a sensitivity to anxiety and an easy capacity to regress readily into psychotic pictures" in later life (10).

It was reasoned that if Bender's theory is correct, the basic physiologic immaturity should distinguish potentially schizophrenic infants from their normal peers before the more readily recognizable psychological and social symptoms appear. Thus, if one examined a random sample of infants and selected those who showed the characteristic signs of immaturity and uneven development listed above in 1) to 5), these infants should prove to be those most vulnerable to schizophrenia. The following pilot study was planned to test this hypothesis on a small scale before launching a more elaborate investigation. It was hoped that longitudinal study of such infants would also illuminate some features of the nascent schizophrenic disorder and indicate directions for more detailed study in the future.

II. Procedure

A. *Collection of data*

In the winter and spring of 1952–1953, 16 infants under 6 weeks of age were picked at random from those admitted to a well baby clinic. They were followed on successive well baby visits as long as possible up to the present time. In addition to the regular regime followed by the clinic pediatrician, the author examined each baby and mother (and a few fathers who were available) at each visit. Data were accumulated in the following areas by interview and observation, combining detailed pediatric, developmental, neurological, and psychiatric examinations.

1. *Family:* Past history of parents and relatives; interaction of parents with each other and with the child; current problems, tensions and environmental difficulties, as these were reported spontaneously, supplemented by questioning. Direct psychiatric evaluation of mother and any other members of family who were available.

2. *Infant:*

a. *Medical history* of birth and intercurrent illnesses.

b. *Physical development:* physical appearance, height, weight, circumference of head and chest.

c. *Homeostasis.*

1) Temperature response to illness, immunizations.

2) Vasomotor status on inspection; presence of pallor, mottling, cyanosis, flush, dermatographia.

3) Respiratory and gastrointestinal symptoms; response to hunger, feeding, new foods, toilet training.

4) Allergic phenomena.

5) Sleep pattern and clinical evaluation of over-all activity level; somnolence, lethargy, wakefulness, irritability.

d. *Motor.*

1) Muscle tonus on palpation. This normally becomes firmer as the child grows older and was here evaluated as soft or firm by clinical comparison with normal infants of the same age. The extreme of the molluscous muscle tone or doughiness which Bender has demonstrated in schizophrenic children (7) may be felt in Mongolian idiots.

2) Activity drive; noted roughly whether in the upper or lower range for age in initiation, speed and persistence of activity.

3) Postural tone and development of locomotion, evaluated according to Gesell's tests of Motor Behavior (27); clinical estimate of axial muscle tone on passive manipulation; presence of tonic neck reflexes.

4) Physical compliance; conforming to positions induced by being held or passively manipulated by the examiner. Normally this gradually decreases as the child grows older and develops independently-maintained erect posture,

except during extreme physical relaxation or affectional cuddling. Later, physical compliance overlaps other elements of social relationship. The extreme of compliance, pathological for that age, is seen in the cerea flexibilis of certain adult schizophrenics, or in the "melting" described by Bender in schizophrenic children (5).

e. *Perception:* noted roughly whether responsiveness to external stimuli was in the upper or lower range for age; organization of sensory data into an awareness of self and environment (overlaps *Social*, below).

f. *Language:* evaluated quantitatively according to Gesell (27), and qualitatively by history and observation.

g. *Social development:* estimated quantitatively up to 2 years of age according to Gesell (27), plus qualitative observation of:
   1) Identification of self: body image as seen through verbalizations and actions; relation to objects, space, time, movement, gravity.
   2) Relation to parents, siblings, outsiders, strangers.

h. *Anxiety and defense mechanisms:* clinical estimate of early irritability and apathy, and later moodiness, fears, neurotic symptoms and withdrawal; especially noted how fully child exploited his own capabilities, related to others, to new situations, developed constructive patterns, etc.

B. *Analysis of data*

Quantitative. Height and weight were charted on the Wetzel Baby Grid and compared with Wetzel's standardized "channels" of height-weight ratios, and his norms of over-all body growth ("auxodromes") (33). Developmental examinations were charted on standard Gesell forms under his categories of Motor, Adaptive, Language and Social Behavior (27). These indices were then graphed so as to visualize the over-all pattern of development in each infant (figs. 1–4). The data were not graphed until the children were 2½ years of age, in order not to prejudice the early observations. The chronological age of the child at examination was plotted on the abscissa. The developmental status when examined was graphed individually for each function on the ordinate. For the purpose of comparing different functions, the level of development in each area was expressed as the chronological time when it normally appears in Gesell's or Wetzel's schedules (e.g., "walks with one hand held" was plotted on the Motor graph as "12 months"; and the rating for combined height-weight, equivalent to Wetzel's "level 35" was plotted on the body-growth line as "12 months"). The developmental status was plotted accurately to the nearest month in the first year, the nearest three months in the second year, and the nearest 6 months thereafter. Growth in head circumference was reduced to Wetzel's chronological norms, but was only plotted from birth to 18 months of age as the increments per unit time after that age were too small to be compared accurately.

The developmental graph for each infant provided a rough visual picture of the internal symmetry of development. When the longitudinal rate of development of a single function was fairly constant, this was seen in its even curve. Conversely, successive regressions, arrests and accelerations could also be seen pictorially. When the several areas progressed in unison, they formed a symmetrical series of curves. When development at any age was uneven in the several areas, the lines spread and crossed haphazardly, producing a visually chaotic pattern.

Qualitative. At the time of the first examination at 4 to 6 weeks of age, each infant was diagnosed as being "vulnerable" or "non-vulnerable" in accordance with Bender's criteria for physiologic immaturity and uneven, or plastic, development in schizophrenic children. On later examinations, impressions were recorded of changes in the physiologcal stability as well as the over-all clinical impression of the child's and his family's adjustment.

III. Results

On their first examination at 4 to 6 weeks of age, three infants were identified as being "vulnerable". A fourth was considered normal at 6 weeks, but was diagnosed as "vulnerable" at 4 months of age. The detailed records of these 4 infants are summarized below, in the order of decreasing signs of "vulnerability".

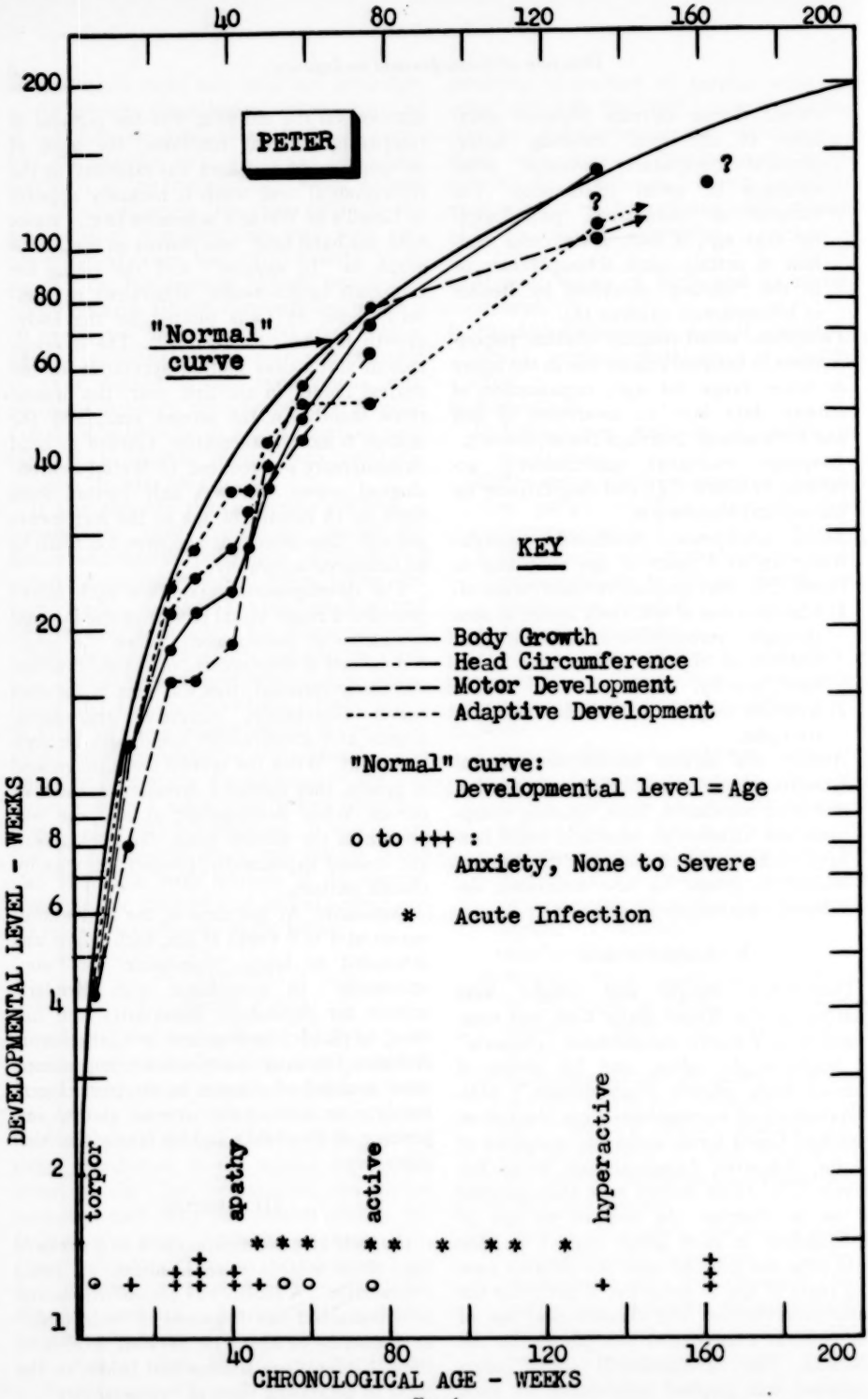

PETER
"Normal" curve
KEY
Body Growth
Head Circumference
Motor Development
Adaptive Development
"Normal" curve:
Developmental level = Age
o to +++ :
Anxiety, None to Severe
* Acute Infection
torpor
apathy
active
hyperactive
DEVELOPMENTAL LEVEL - WEEKS
CHRONOLOGICAL AGE - WEEKS
1
2
4
6
8
10
20
40
60
80
100
200
40
80
120
160
200

FIG. 1

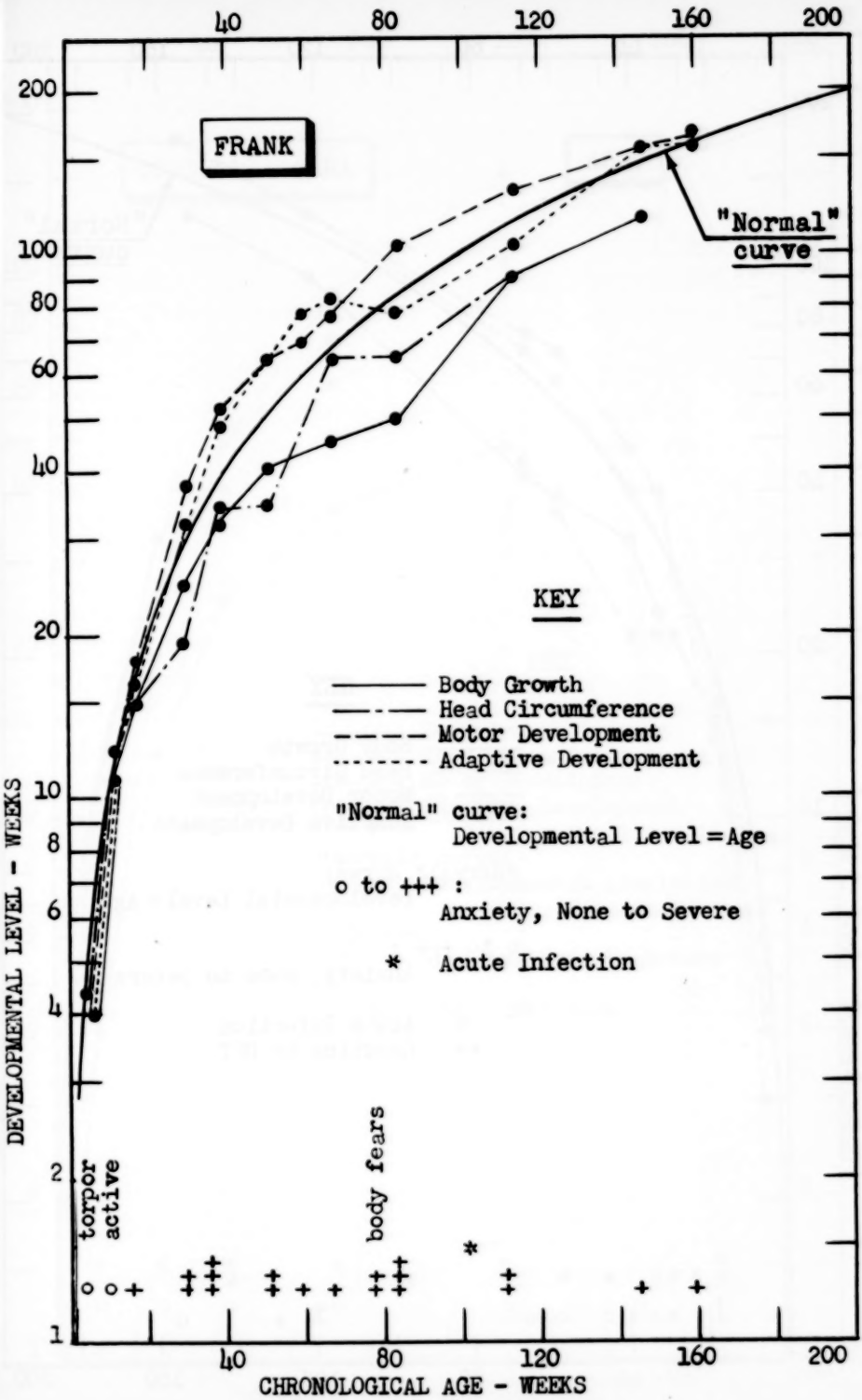

FRANK
"Normal" curve
KEY
Body Growth
Head Circumference
Motor Development
Adaptive Development
"Normal" curve:
Developmental Level = Age
o to +++ :
Anxiety, None to Severe
* Acute Infection
torpor
active
body fears
DEVELOPMENTAL LEVEL - WEEKS
CHRONOLOGICAL AGE - WEEKS
1
2
4
6
8
10
20
40
60
80
100
200
40
80
120
160
200

FIG. 2

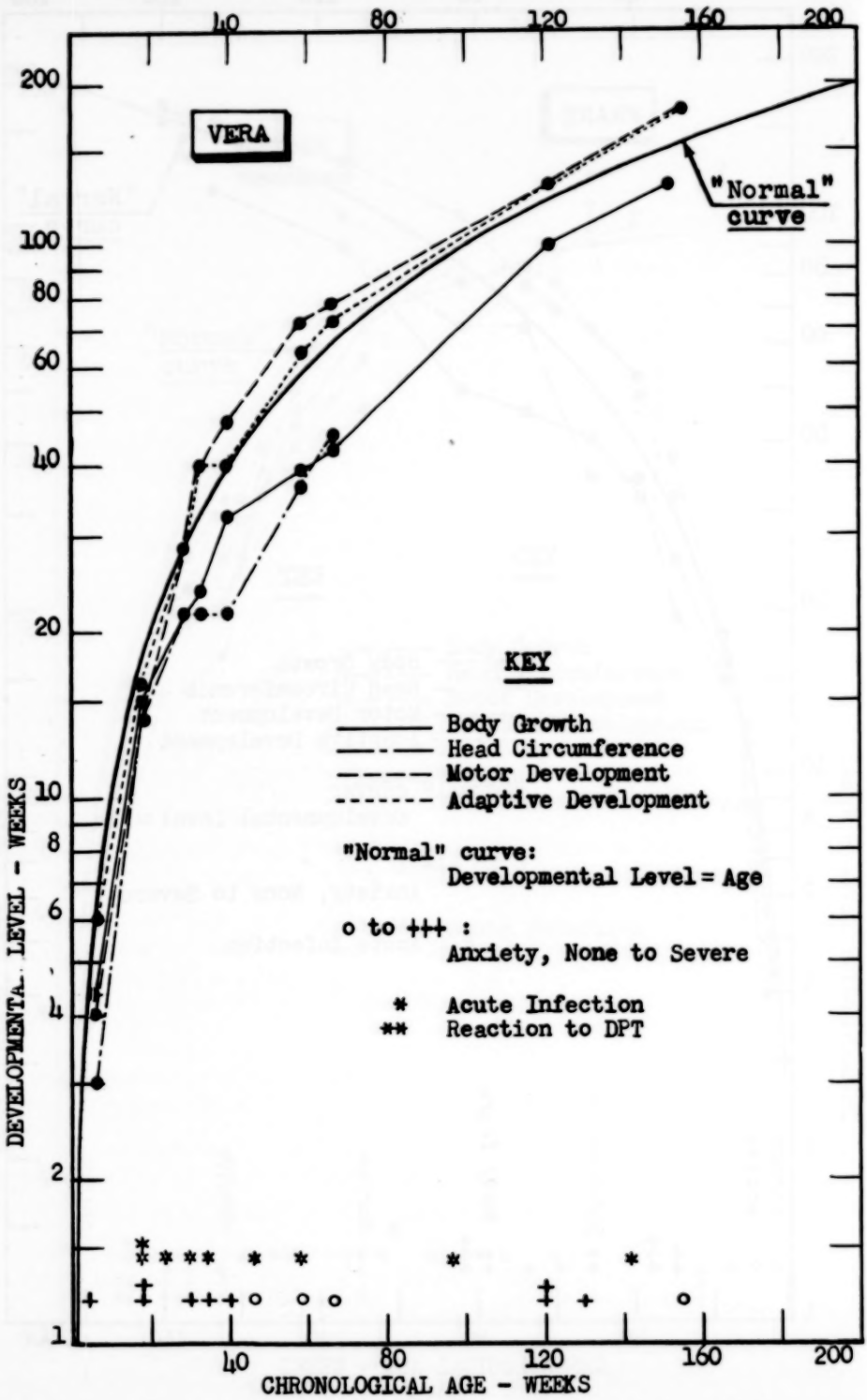

VERA
"Normal" curve
KEY
Body Growth
Head Circumference
Motor Development
Adaptive Development
"Normal" curve:
Developmental Level = Age
o to +++ :
Anxiety, None to Severe
* Acute Infection
** Reaction to DPT
DEVELOPMENTAL LEVEL - WEEKS
CHRONOLOGICAL AGE - WEEKS
1
2
4
6
8
10
20
40
60
80
100
200
40
80
120
160
200

FIG. 3

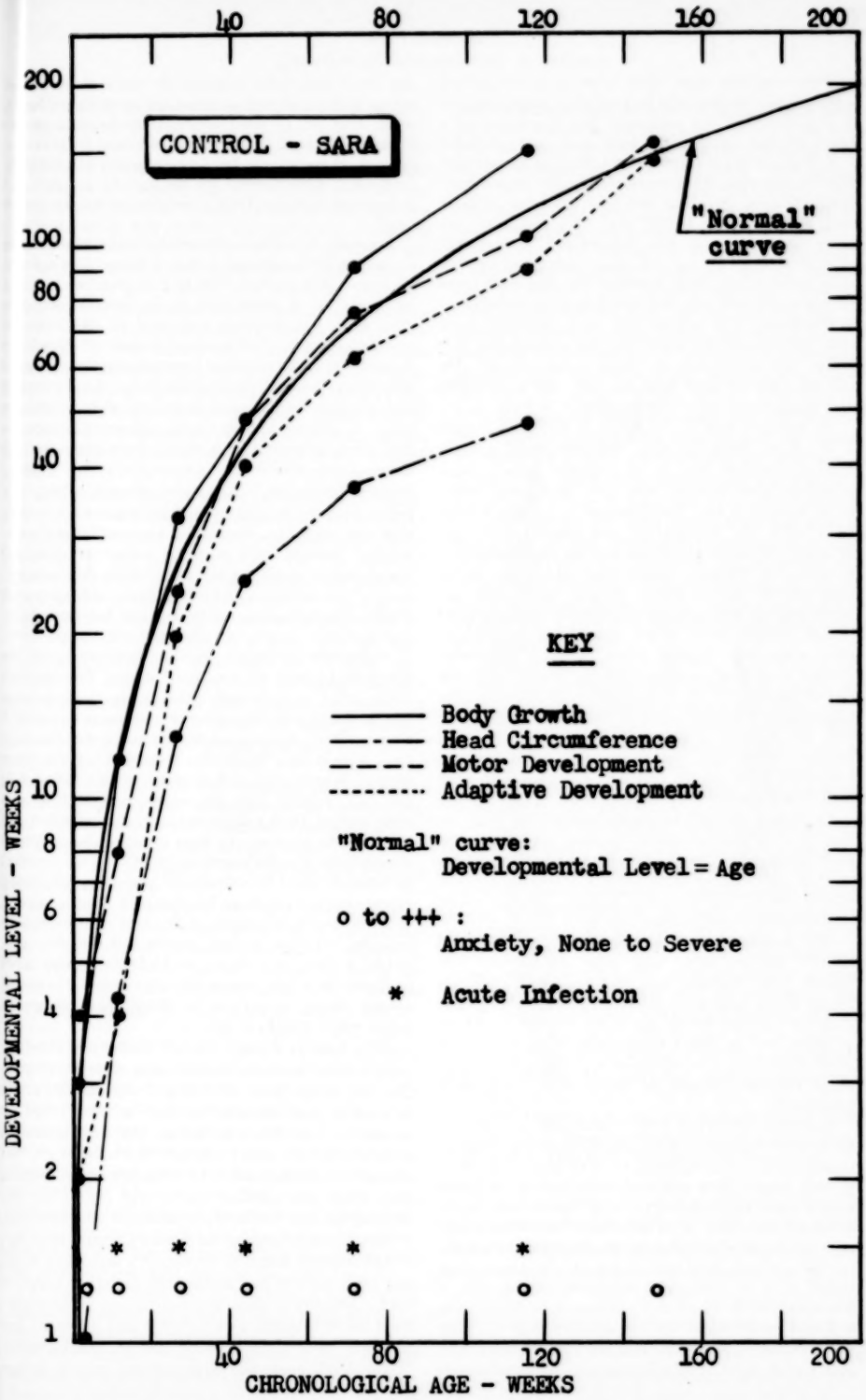

CONTROL - SARA
"Normal" curve
KEY
Body Growth
Head Circumference
Motor Development
Adaptive Development
"Normal" curve:
Developmental Level = Age
o to +++ :
Anxiety, None to Severe
* Acute Infection
DEVELOPMENTAL LEVEL - WEEKS
CHRONOLOGICAL AGE - WEEKS
1
2
4
6
8
10
20
40
60
80
100
200
40
80
120
160
200

FIG. 4

Peter was the third child born to a 35-year-old schizophrenic mother who had required hospitalization several times for her psychosis. She functioned at a below-average intellectual level and had attended C.R.M.D. classes in public school. She was hospitalized first for one year at 19 years of age. She required rehospitalization for about one year after the birth of each of P.'s silbings in 1947 and 1950, and again became psychotic and was hospitalized immediately after P.'s birth. P. and his older sister and brother were cared for by their grandmother. She gave them adequate physical care but was herself an ambulatory schizophrenic. She related only on a superficial level and was considered "dull" by the community. P.'s father was known only to "have a bad temper". He left the children each time his wife was hospitalized and disappeared permanently after P.'s birth.

P. was first seen at *5½ weeks of age*. Birth weight 7 lb., 3 oz. Birth full-term and uneventful. Grandmother described him as "a beautiful baby". Slept promptly after feeding, was very quiet and didn't move around in bed. On examination he was a large baby with fair, transparent and mottled skin. Developed cyanosis of the hands and the circumoral zone after crying. Doughy muscle tone. Much less active than normal. In the supine position hands were unfisted and legs were held extended rather than the usual flexion. Showed none of the usual brisk movements, only some mild kicking when he cried. Otherwise showed only slow, writhing fish-like motion of trunk and extremities. In the prone position made no crawling movements. Postural tonus of the trunk was so soft that he couldn't be pulled to a sit, but had to be literally "folded up", yet he was able to lift his head and chest when prone, and held his head with very little bobbing when body was supported sitting. Showed a diminished response to sounds, voices, and light. At that time he was considered to show abnormally uneven development, with head control advanced for his age but with marked immaturity of vasomotor control, muscle and postural tonus and motility, and diminished exteroceptive responsiveness (fig. 1).

3½ months. Quiet, "sleeps all day and cries all night". Marked pallor and waxy complexion. Soft muscle tone. Postural tone had regressed: could no longer lift his head when prone. Eye-hand development continued normal for his age in his reaction to objects in space, but he didn't regard objects he held in his hand. Expression was impassive with diminished vocal-social response, though he smiled after much vocal stimulation.

6 months. Disturbed sleep. Cranky all day and had an increased appetite. Now cried after eating. Became constipated, producing stools in small hard balls. Body growth lagged. Was pale and waxy-looking with soft muscle tone. Lay inactive prone or supine; was flaccid and inert when held. Most prominent was his decreased postural tonus which showed an exaggerated cephalocaudad gradient. Held head in line with his trunk when pulled to a sit and when supported sitting, like a five-month baby. Trunk and legs were more flaccid than a 3 to 4 month baby: he flopped over from a sitting position flat on his face, and his legs crumpled and didn't push down at all when he was supported standing. Tonic-neck reflex persisted. He curled his toes when supine and curled and uncurled his outstretched hands when held up, in what appeared to be attempts to increase the tone in his extremities and to maintain balance. However, eye-hand development and manipulative skill were normal for his age: he grasped and transferred adeptly. Didn't vocalize except to cry or laugh.

7 months. Irritability, gastrointestinal symptoms, lag in body growth, postural tone and motor development increased. Was no more able to hold trunk or legs in a supported sit or stand than at six months, and now cried as he wobbled in a supported sit. Held himself in hyperextension when supine or supported upright, as if vainly trying to maintain tone and position. Relaxed only when cradled in the examiner's lap; then he melted and became inactive and curled up like a newborn baby. No increase in deep tendon reflexes; withdrew his legs when supported in a stand. In a supported sit manipulative ability was quantitatively only slightly retarded for his age, but he stared solemnly a long time before reaching for objects, and his approach was very slow and tentative. Moved his arms stiffly and awkwardly; hovered over a block before grasping it; transferred it, mouthed it, banged it in slow motion; stopped to scratch it with his forefinger and inspect it at length. His expression was serious and non-responsive, and he didn't vocalize at all in the office or at home.

9½ months. Evening irritability diminished, but "he wants to be held all the time" during the day. No longer cried or indicated when he was hungry; was unable to suck milk from a bottle, and had to be fed with a spoon. Body and cranial growth and motor development were at their lowest ebb, about 4–5 months below normal. Was inactive and apathetic with mottled skin and cold, reddish feet. Decreased postural tone was most marked. Only a slight residual hyperextension was noted in his tendency to keep his toes plantar-flexed when supine. Couldn't seem to make his body do what he wanted; cried in unbalanced positions even lying down; couldn't roll from his side to a prone position. Reaching and manipulative ability were only one month retarded but were in slow motion and dreamily performed without any vigor or enthusiasm. Several times he stared for a long time at his empty hand, turning it around slowly, a pattern he should have outgrown before seven months of age.

10½ months. Brought by his mother who had returned from the state hospital three days previously. She was much more affectionate and responsive to P.'s needs than his grandmother had been, and he seemed to find this comforting. She was somewhat anxious when he didn't perform on examination, but this only made her active in stimulating and helping him, which the examiner encouraged her to do, explaining his need for active stimulation and direction.

In the month prior to his mother's return, however, P. had suddenly begun to develop at a rapid rate. Head and body growth had accelerated despite a series of colds. Difficulty in sleeping occurred only occasionally. Held his own bottle. Postural tone had increased but was still abnormally soft on passive manipulation. Motor development had advanced two months in four

weeks, and he was now able to sit alone with a straight back, although he was a little unsteady and cried.

11½ months. Development continued its rapid progress. No longer had trouble sleeping. Took solids, but choked with a cup. Skin still pale and mottled, but muscle tone was less doughy. Postural tone had improved, but he still cuddled and melted like a younger infant when held. He had advanced two months in one in both locomotion and manipulation. Had begun to creep and to pull himself to a stand but was still anxious with an unsteady equilibrium even when supported erect. Play became more active for the first time although it was slower and more deliberate than normal. Crawled after toys to mouth, shake, bang, match, poke and throw them, etc. Had learned to clap hands in his first imitation of gesture. Didn't seem to understand any words yet, but was sensitive to changes in his mother's tone of voice, crying if she sounded stern.

13½ months. Despite severe colds and otitis media, locomotion and body growth continued to advance at an accelerated rate and were now only about one month retarded. Muscle tone still doughy but skin color was good for the first time. Walked unsteadily with one hand holding his mother or the wall, but his legs still looked rubbery and he whimpered when he swayed. He had begun to mimic and enjoy play with his older brother. For the first time made sounds other than crying and laughing; these were at about the nine month level, although he didn't exploit his ability to mimic sounds as much as the normal baby at that age would have. Play was still mostly serious and deliberate, but for the first time he smiled responsively at the examiner durying play, and shook his head to refuse something. In the four calendar months between 9½ and 13½ months, he had progressed from being able to sit at a 4 to 5 month level to being able to walk like a 12 month old. His lagging body growth had shown a similar acceleration.

18 months. Locomotion and body growth were at normal levels, far outstripping the rest of his development. Spontaneous behavior was active and happy. Was preoccupied with walking, running, throwing and chasing toys to the exclusion of all other types of activity. Language and manipulative ability had advanced minimally. Only said, "mamma" and "baba" like a 9 month old. Wouldn't play with blocks, pellets, crayons or other toys at home or on examination, except for a ball. Laughed excitedly at a rolling ball, yet when it rolled under a chair, behind something, or in an unexpected direction, though it was plainly visible and within reach, he looked at it and cried as if it were unattainable, and got his mother to get it for him. She reported that he "was shy and turns away from strangers" and "cries if he can't get something". On examination he smiled and played with his mother, but for the first time he avoided any interaction with the examiner and cried when he was picked up.

31 months. Mother seemed less harried and anxious, and more "absent". She looked about 5 months' pregnant but evaded any discussion of this.

P. was "active", "wild", and "mostly ran around" although he played with dolls a little and showed some domestic mimicry at about a 24 months level. His only play with other children was to "wrestle" and he had been hurt several times. Had begun to say a few words at 27 months of age and then said three word sentences at 29 months. Indicated his needs with gestures like a 21 to 24 month child. Talked to his mother and to children but was very fearful of strange adults and would talk to no adult other than his mother.

He was a good looking boy with good color, doughy musculature, transparent skin and doll-like features. Had a constantly sad, anxious expression. Was shy, clung to his mother, and crawled into her lap. Responded to complicated directions, but wouldn't answer questions, name objects, etc. Spoke three to four word sentences into his mother's ear. His only spontaneous play was with a ball. Approached all other toys tentatively, requiring much encouragement and direction before he seemed to get the idea of what was wanted. Manipulation of blocks was dreamy and only at a 24 month level. He couldn't seem to get the concept of different directions in space and built only vertically, not horizontally. Yet hand coordination was good for his age: he became absorbed in trying to hold a pencil in his fingers with an adult grasp and persevered until he mastered this. Only then did he scribble. He was unable to imitate figures at a 24 month level, but after his hand was guided once, he repeated designs expected of a 30 month old.

Development was still uneven. Body and cranial growth were normal but muscle tone was doughy and infantile. He now lagged in language and social adjustment more than in manipulation and locomotion. There was some indication that he was uncertain about his orientation in space; he was fearful and hesitant in his relationship to the outside world and extremely dependent and clinging on his mother.

37 months. P. was brought by his grandmother. His mother had been in the state hospital again since he was 33 months old, and she had given birth to a boy one to two months after admission. The grandmother had been caring for the children. P. was even more anxious and withdrawn than he had been six months earlier. At home he ran around aimlessly, played poorly, threw and broke toys. He didn't play with his brother or other children, was "very scared, shy, all the time". Had "bad temper tantrums, kicks and screams". He was reported to feed and toilet himself and to speak in sentences. He was very fearful in the office and clung to his grandmother. He didn't play with any toys, books, crayons, etc. whether he was left alone with them or when encouraged. He cried and buried his head in his grandmother's lap when approached, and said, "Don't wanna play with toys. Wanna go to house."

P. is considered to be a schizophrenic child who has excessive anxiety, and major problems in identification and relationships, but who is not psychotic or unreachable at the present time. His entire development has been very aberrant, with every area of functioning being affected at some time. Early he was torporous with fetal motility; later his postural development lagged, and he became

apathetic and irritable. Since 18 months of age he has been hyperactive, impulsive and extremely anxious in relation to people and his environment to the degree that it is impossible to estimate his intelligence adequately. His play is disorganized and his fine manipulation appears to be below normal; however, he is apparently capable of speech at his age level.

This cannot be explained as being merely mental retardation. His growth has included unusual acceleration as well as retardation. His functioning at any one time has been characterized by wide scatter, of the type not seen in ordinary retardation. There have always been one or more functions which have shown him to be of at least low average potential; at first adaptive behavior, and later locomotion and speech. Nor does this picture fall into any of the usual categories of neurological disease. P.'s disability in postural control and locomotion was a temporary one which disappeared by 18 months of age. Since that time he has had no signs of any focal disorder.

He appeared to suffer more from his primary physiologic immaturity because of the inadequate mothering he received. In infancy he showed special needs for increased physical support and social stimulation, and since then he has needed special help in establishing patterned behavior and social relationships. His mother, and more especially his grandmother, have been almost totally unable to meet these needs.

Frank was the first child born to a 30-year-old unmarried mother. She discovered she was pregnant after a brief affair had already been terminated, but insisted on having and keeping the baby because she "had always wanted a large family." She was intelligent, lonely and rather timorous person who had had four years of college and worked as a secretary. She stayed home receiving public assistance in order to care for F. On the whole she was a good mother, sensitive and responsive to F., and she enjoyed him after the first 2 weeks after some anxiety about her competence had passed. She described Frank's father as "not very stable. He hasn't stuck to anything. He didn't like being an engineer and is now back in postgraduate school," in another state. He never had any contact with F.

5 weeks. Birth weight 6 lb., 15 oz.; birth full-term and uneventful. "He slept constantly", for the first week, had to be awakened for feedings. Still frequently sleepy after the first five minutes at the breast and cried very little. Did not move much and always held his left leg out. Smiled at one week of age. On examination he was a pretty, small-featured baby with an unusually prominent overhanging of the upper lip, mottled skin, and doughy muscle tone. Abnormally inactive. Lower trunk and legs turned to the left and resumed this position after passive correction, but motor and postural development were otherwise normal, in fact, head station was somewhat advanced. He turned his head toward the examiner's voice and face with a social smile advanced for his age. At that time he was considered to show abnormally uneven development, with decreased muscle tone and activity in the presence of normal head control and advanced perception and social responsiveness. He was x-rayed for a possible orthopedic deformity of the left hip and was found to have a congenital dislocation. (The latter was treated with light splints and was normal clinically and by x-ray by six months of age (fig. 2).)

2½ months. Had become extremely active, laughing and kicking. Muscle tone still soft but skin showed no mottling. Motor, postural and manipulative development at his age level or slightly advanced. Followed objects and people normally with his eyes and head, with the exception that he did not look at his own hands, even when holding something. He was "so busy looking around, sometimes he can't nurse. He practically jumps out of my arms when he sees the 'baby' in the mirror."

4 months. Began to cry and have difficulty falling asleep at night but was otherwise well. Pallor and soft muscle tone were the only abnormal findings on examination. Increasingly active, with head and trunk control in a sitting position advanced one month or more. Manipulation, language and social behavior were average.

7 months. Sleeping difficulty now marked. Body and cranial growth began to lag. Skin sallow and mottled. For the first time, he showed difficulty in postural control, and uneven motor development: when supine he couldn't roll to a prone position and cried when on his back, unlike the average 6 month old. Yet he had been able to sit up by himself from the age of five months, now pulled himself up to a standing position, and was otherwise about two months advanced in locomotion. Extremely active. "He always tries to do something ahead of himself and gets frustrated and cries when he can't." Adaptive behavior was at his age level.

9 months. Postural tone normal except for an exaggerated lumbar curvature more appropriate to 7 months. Very active, walked with support like an average 12 month child; tossed a ball and toys forward and backward over his shoulder, chased them. Manipulation was at about a 10–11 month level although he frequently poked with his thumb rather than his index finger. Language at his age level; was friendly and "flirted" with strangers. "He's fascinated by people's feet. He likes to pat and talk to his image in the mirror, then looks behind the mirror." If held by his mother in front of the mirror, he looked at his mother and her image and "looks puzzled". "If he couldn't creep under a low chair, he wouldn't seem to understand before that he could put his head down. Now for the first time he does."

After a 6 week hiatus, sleeping difficulty had become

extreme for 2 hours at night, without any other symptoms. He was given elixir of benadryl at bedtime. With this medication he fell asleep promptly and became less cranky during the day time.

One year. Bedtime irritability returned whenever benadryl was stopped. Lag in body growth had become marked. Muscle tone soft. Slight circumoral cyanosis. Active and responsive. Walked like a 13 month old. Manipulative development at a 15 month level, but his use of speech was retarded. He squealed but rarely mimicked sounds and didn't say "mamma". He had no hearing defect and was able to enunciate. He had said occasional words appropriately since 10 months of age but then dropped each word after one or two trials, e.g., "stop it", "bye-bye", "teddy", and "how-do", and "ta ta" (for thank you). He occasionally still said "hi" or "ga" (for thank you). "He sometimes makes sounds like he's trying to tell me something."

13 months. Slept better without medication. Used a spoon, but when he drank from a cup he drank from the opposite edge, or tried to drink from the bottom. Toilet training had not been attempted as he was "too irregular", but "a couple of times recently when he had a bowel movement without diapers on, and once in the bathtub, he started to cry. He seemed frightened of it and didn't want to play with it, although he enjoyed playing with it a few months ago."

14 months. Mother was under tension because of indecision about financial and other matters, but was able to use her lawyer and examiner for support. F. slept well, rarely required medication. He seemed happier and friendly. Language had caught up: he said several words and babbled more. Recognized and patted pictures. After scribbling on paper, he examined the other side of the paper.

15½ months. Occasionally required medication to sleep. Body growth lagged. Sallow and doughy. Otherwise development was quantitatively at a high point: motor, adaptive and language behavior were at about an 18 month level. He had a strong motor drive; he ran, stamped, walked on tiptoes a lot, frequently walked backwards and experimentally banged up against doors and walls. Still tended to drop words he had acquired and not use them again for weeks. Very easily discouraged in manipulative tasks if he didn't immediately succeed. Played with other children but was shy with strange adults and cried when anyone approached. Was confused by transparent containers: tried to push a pellet through the side of the bottle before dropping it in. Was frequently confused at home by objects inside of plastic bags, etc.

19½ months. Following his return from a happy, active summer he showed a marked increase in anxiety. His mother's disposition and social situation had been stabilized for some months, but she became very concerned at the change in his behavior. She wondered why he was upset and had "gone back to his baby behavior." She wanted help, and for the first time was able to accept a referral back to her original family agency. She had previously avoided them feeling that they exerted too much pressure on her to put F. up for adoption.

F. was unable to sleep without benadryl. Cranky much of the time, wanted to be held a great deal and twirled his hair and sucked his thumb so hard he produced a callous. Wanted to be fed again and to be held to eat. Whined readily with slight frustration. He had been fearful when tried once or twice on a training seat, so this was discontinued. Sometimes fearful when a toilet was flushed nearby. "He just wants to run around. He doesn't play with toys. What is the nature of his speech? imperfect imitation or just noises?" On examination he was very anxious and withdrawn. Body growth at its lowest point. Skin sallow and mottled, muscle tone doughy. Locomotion at a 24 month level, but he failed at some manipulative tasks that he had performed 4 months earlier, and refused others. Language had also regressed. He was capable of saying, "Close the door", but otherwise only chattered jargon to himself. When he wanted something, he pointed and sometimes grunted. He looked unhappy most of the time and only smiled during solitary play and when thrown in the air. He cuddled and melted into the examiner's lap like a much younger child, though he whimpered at the same time.

26 months. Since the previous visit the mother had been seen weekly by a social worker at the family agency and felt that things were "straightening out". F.'s anxiety had been at a peak from 20 to 22 months. "He was terribly frightened of a bath, and even if his knees were washed with a cloth; he seemed to be afraid something would happen to him. He asked worriedly about everything 'Where it go?' It upset him: The bath water draining, a ball under the table, if he didn't see someone." After 22 months these fears subsided although he still needed medication to sleep. He sat on the toilet without fear, but "had no interest in it", and still used diapers. "He's very imaginary. Frequently points to things that aren't there: a chicken, teddy bear, etc. or calls something in a book what it's not. Somethimes it takes many repetitions before he identifies it properly. He plays with an imaginary companion, chatters in his room 'this yours, this mine, go away', etc. and sometimes he fights with 'him': when F. slid off his big toy dog, he screamed furiously and had a tantrum, saying, 'he' had pushed him off." He had several friends and entered play with other children in the park, offering his toys. He rode a tricycle at 23 months and was still more advanced in the motor area than others, but development was more in balance than 6 months before.

His face looked pinched with deep rings under the eyes, but he was much more outgoing than the previous examination: active, busy, playing, and talking about his immediate experiences. Still related physically like a much younger child, and has always "melted" when held in the lap. Rate of body growth had begun to accelerate for the first time since 7 months of age, despite several recent episodes of otitis media and diarrhea. Manipulative skill and language were approximately at a 24 month level. Used pronouns correctly but sometimes echoed simple questions without appearing to realize that an answer was wanted. He persistently wanted the examiner to "see chickee" outside the window in the empty sky and seemed puzzled that this was not confirmed. Later it "went away, gone" and then reappeared several times. It was not used as an attention-getting device but did appear

to be some kind of experimentation with the world and another person's reactions.

33 months. Behavior better integrated, with less anxiety than 6 months before. Played cowboys with his real friend and his imaginary companion; chasing, shooting, wrestling with great pleasure. Played by himself, using blocks and cars in an organized fashion. Performance in all areas approximately at a 36 month level. Speech had caught up and he was more communicative than before.

His mother was pleased that he communicated and related better, but she felt "unable to keep up" to his constant running around. He resented having to be still for dressing, eating, etc., and she usually took the path of least resistance, but sometimes became very impatient with him. He drank milk and juice only from a bottle and his mother felt unable to influence this or to institute toilet training, despite help from the examiner and the case worker during the previous year. He wasn't fearful of the toilet, but defecated only in his diapers. He resented being interrupted for changing, but afterwards seem to enjoy "clean panties". He pointed to dogs "b.m.", but called his own feces "pants".

On examination, muscle tone was less doughy than before, but he was very sallow. He showed independent initiative as well as adequate interaction with the examiner. He was goal directed and interested in materials but could be shifted by offering new materials. He refused to copy a circle (which should be copied at 36 months), but imitated a cross at a 36 month level. There was a hint of fluidity in his perception when he named pictures: the first picture of a "doggy" colored all the subsequent identifications ("doggy's coffee" for a cup, "doggy's shoe, doggy's house, doggy's star, doggy's flag," etc.).

37 months. His mother felt inadequate to deal with F.'s increased negativism and hyperactivity, with some justification. In his running and jumping off high places, he had knocked out one front tooth. His attempts to wrestle with other children in the park had made him unpopular with their mothers.

On examination he was pale with circumoral cyanosis, but tissues didn't feel doughy, and he didn't melt in the examiner's lap. However, although he smiled and related to the examiner promptly with much pleasure, and played independently with toys, he showed an oblique negativism throughout the exam, quite different from his response at 33 months. His attention span was shorter. He evaded most items by darting off to do something else. He enjoyed naming many single items with their action in a picture dictionary, but given a large picture he pointed to the several inconspicuous "little birdies" and ignored the prominently pictured children, even when asked about them. Drawing had regressed: returned to holding a crayon in his fist and refused to copy a circle, cross, etc. He called a few spontaneous strokes "rain" (it was raining outside). He eventually followed several directions about placing a ball under a chair, etc., but instead of putting "the ball on the chair", he got onto the chair himself, holding the ball, and couldn't seem to understand what was meant. In marked contrast to most of his behavior, he responded quickly and beyond his age level to the formboard and color forms: placed all of them instantaneously and correctly without any apparent thought. These were the only materials other than his cars that he exploited spontaneously, saying later "want to do puzzle again."

F. is an engaging but difficult child who is advanced verbally and in some areas of performance. However, he is emotionally very immature and negativistic, has a poor identification of self, and an abnormally low threshold for anxiety. His development has been moderately uneven. Very early he was inactive, but he has always been hyperreactive to stimuli. Language and motor development were alternately retarded and precocious. Perceptual organization was fluid and sometimes confused. He has had long periods of increased tension and irritability in infancy and since, the worst being from 18–22 months. At that time he became withdrawn, autistic, simultaneously clinging and negativistic, and was terrified by fears of bodily harm. He has improved somewhat since then. His mother's need to cling to him and her inconsistent efforts to establish limits for him have perpetuated his difficulties in establishing his own bodily boundaries and more mature behavior patterns.

Conrad was the first child born to a couple in their 30's. His mother had had two previous miscarriages. She had been a staff nurse, but remained home to devote herself to C. She impressed the examiner as a "warm, intelligent woman who wanted to use the examiner to spill her preoccupations about her mother and husband, although she didn't acknowledge these as problems. Full of joyous detail about baby, who seemed to represent a neurotic fulfillment rather than a burden. She was nursing on demand, and the only suggestion of inner difficulty was her feeling that she 'couldn't keep up to him,' although she had plenty of milk. In the evenings he 'had to be nursed on and off every one to two hours'". C.'s father was reported by the mother to be a "silent man" who received a 50% disability from the army on unknown psychiatric grounds, and was working for his B.A. in social studies under the G.I. bill.

4 weeks. 7 lb., 7 oz. full-term baby, born by Caesarean section because his mother had been treated for a mild preeclampsia during her pregnancy. No neonatal difficulties. Mother felt that a few days before visit his "scope of awareness had enlarged" and he now attended to her voice and face.

On examination he was an alert baby with small features and a pinched-looking, grown up face; very prominent snout-like upper lip and intent blue eyes. Skin was pale-white, but turgor not remarkable. Activity normal in amount, but tended to be slower than normal and "stretchy" rather than the usual

kicking and thrashing. Head control normal in prone, but didn't push with feet or "work" at lifting head. Tonic neck reflex more easily elicited and more prominent than usual. Alert and responsive to visual and auditory stimuli to the extent that "even when quiet he did not look at peace."

Infant was considered to show mild signs of vulnerability because of pallor, hypoactivity and immature motility, in the presence of normal postural development and increased sensitivity to stimuli. Mother was erratic in her visits thereafter, and neither she nor the patient was seen by the author in the following months.

2 months. Clinic pediatrician noted "good progress. Mother nursing." Mother asked nurse to write down instructions: "believes she may not be doing things right. Complains of feeling tired, child up every two hours during the night playing, not crying. Husband leaving town to help his family" in another state.

4½ months. Mother insisted on being seen without appointment. Pediatrician noted child was "moderately hyperactive. No problems." Nurse reported mother as being "tense, apparently nervous".

8 months. Mother broke appointment, reported she was ill. Clinic terminated the case one month later after finding she had moved to unknown address.

Finding the above comments in the chart, the author suspected the mother might have developed a post-partum psychosis. A check revealed that when C. was *10 months old*, mother was admitted by ambulance to a psychiatric hospital. She had broken the window of her hotel room and threatened to throw the baby through it. She was excited and hallucinating, shouting scrambled delusional ideas. In the course of this she was reported to say, "I love C., but he gets in my way. . . . I want to go into medicine and help people, and I can't unless I have my time to myself." She was transferred to a state hospital with a diagnosis of paranoid schizophrenia.

Vera was the first child born to a Puerto Rican couple in their late 20's. V.'s mother had a bright, cheery facade, but on probing, her thinking was contradictory and revealed a deep confusion in identification. Her relationships, although superficially normal, had an "as if" quality. She was "happy" when she found she was pregnant, although she had "headaches and a pain in her throat like a bone so she couldn't swallow." One month after conception her husband revealed that he was still married to his first wife, and he spent the next year in jail for bigamy. V. and her mother lived with the maternal grandmother, a warm and accepting person who enjoyed V. and took over her entire care while V.'s mother returned to work. V.'s father subsequently joined and supported the household and showed an active interest in V. V.'s mother took pride in V.'s accomplishments and in any sign that V. preferred her to the other adults, but she couldn't be bothered with V.'s crying. She continued working and left most of V.'s care to V.'s maternal grandmother and V.'s father.

5½ weeks. Birth weight 7 lb., 2 oz., birth full-term and uneventful. Held her head up and smiled in the second week. Ate voraciously, cried a lot and "wants company all the time, is only quiet when she is held or in a room full of people. She's awake and eating from 11 a.m. to 12 midnight." Stools were hard.

On examination V. was pasty and puffy with doughy muscle tone, but active and alert, with a social smile. Motor and adaptive development were normal for her age, with head station in prone position one month advanced: she lifted her head and chest and looked around. At this time V. was considered to be a normally developing infant. The pastiness, pallor, soft muscle tone and history of irritability were recorded, but were overlooked because of her normal activity and responsiveness (fig. 3).

4 months. Screamed for an hour before falling asleep at night and before day-time naps. Didn't cry when hungry, but ate well when food was offered at regular intervals. Defecated twice daily producing tiny, hard balls, with much crying and straining. Cried unremittingly with strangers, but stopped promptly and smiled with her parents or grandmother. Was fascinated by light and laughed at her reflection in the mirror. Moved around so actively in bed that she had to be enclosed or attended to, but "her head wobbles more than before. She feels like butter."

On examination V. was pale, doughy and postural tone had regressed. Trunk and extremities were so flaccid it was difficult to pull her to the sitting position. Head lagged excessively when she was pulled to a sit, and head control when sitting was 1½ months retarded. Legs crumpled when she was supported erect, having less tone than a normal 3 month infant. However, she responded to blocks with excitement; eye-hand development and vocalization were normal for her age and social responsiveness was somewhat advanced.

At this time V. was considered to show abnormally uneven development with doughy muscle tone, pallor, regressed postural tone and uneven motor development, in the presence of normal development in other areas. Coincidentally, she had difficulty falling asleep and a spastic constipation. Reexamination of the earlier record showed that all these signs had been present on the first examination with the exception of the abnormal postural tone.

One hour after this visit, V. had a severe sensitivity reaction to her first DPT injection. She shivered, had a temperature of 104.8 and purple blotching of the skin. She was hospitalized and studied but no signs of infection were found. Temperature was normal by the third day. Nurses and doctors noted repeatedly that she "was very irritable, . . . didn't do anything without crying . . . irritable when disturbed . . . think she's spoiled."

6½ months. Hospitalized for one week with moderately severe laryngeotracheitis.

7 months. Well, but "still fights sleep. Never seems hungry: could go 5 to 6 hours and never miss food, but when she sees it she gets excited, bounces and squeals and has a good appetite." Constipation had stopped. "She has been trying to sit alone and pull herself to a stand for two months."

On examination she was sallow, legs were mottled, she had blue rings under her eyes and a suggestion of circumoral cyanosis. Motor development still uneven; postural tone had improved but was still retarded. She could sit momentarily with a straight back like a 7

months baby, but began to cry in this position. Head still lagged when she was pulled to sit, like a 4 month baby. Legs were more relaxed than normal when supine, but she held her toes pointing down when supine and when held erect. However, she was active, friendly and vocalizing; manipulative and language behavior were at her age level; social behavior was somewhat advanced.

8 months. Sleeping difficulty only about once a week. "Did everything all at once": crept, pulled herself up to a stand, then sat aone. Was scared the first time she stood, cautious, and cried a little, but then enjoyed it and cruised holding onto the furniture. Muscle tone was still doughy, but postural tone was better. She felt firm and more "discrete" when held. Locomotion was at about a 9 months level, having advanced 2 months in 4 weeks. The only lag in postural tone was seen in an excessive lumbar lordosis when sitting. There was a residual tendency to stand on tiptoe. Manipulative, language and social development continued to advance at her age level.

9 months. Sleeping difficulty about the same. An active, friendly baby. Examination, including postural tone, now normal except for doughy muscle tone and persistent tendency to walk on tiptoe. Walked with support and spoke several words like a 12 month old. Manipulation was only average for her age.

13½ months. Development and personality seemed integrated and balanced. Coincidentally bedtime irritability had disappeared. Appetite was good, but she refused lumpy foods and meat, spat out "anything that tickles, like rice." Body growth lagged, possibly as a result of frequent infections in the previous 6 months. Talked, walked, and ran alone, all at a 15 to 16 month level. Manipulative behavior was at a 15 month level.

15½ months. Continued to develop smoothly with performance in all areas at an 18 month level. Slept well. Still preferred Junior to table foods. Body growth still lagged. Muscle tone doughy. Postural tone was good, but she still frequently walked on tiptoe. Was friendly and talkative with grownups and had begun to play with other children. Had occasional tantrums if kept from doing something she wanted to do.

28 months. Had croup on and off during the winter, in her 21st to 24th months. Increasingly anxious. Constipation and difficulty in falling asleep had returned. Body growth again accelerating, but was still below normal. Motor, adaptive, and language skills all at about a 30 month level, but her over-all patterning was less mature. Was capable of skilled manipulation, but at home "she just runs around, doesn't play with her toys; cries for every little thing, has tantrums if she can't have something; she doesn't want to go to bed at night and sometimes awakens screaming." One such time she ran to her mother, saying, "you choked me," apparently referring to a nightmare, and was afraid to go near her mother that night. Although she spoke three-word sentences and had an estimated vocabulary of 50 words, speech was still very indistinct with much jargon and only "her mother understands her."

Physical examination showed the same combination of infantilism and maturity. She was active, graceful and well-coordinated; she concentrated on the examination and took delight in her achievements. Yet she greeted the examiner, after a year's absence, by immediately climbing into her lap to be cuddled and melted like a small infant.

36 months. Her father brought her and was obviously very happy and proud of her. His relationship with V. was more quietly accepting than was the mother's. He volunteered that his wife was "nervous" and said that when she was impatient, V. "just stayed away." A very active, happy, busy child. No longer had nightmares. Less shy with strangers. Had three colds in the previous winter, milder than before. With the last one she was found to have a marked but transient eosinophilia.

On examination V. was a serious looking girl with sallow complexion, mottled skin and deep rings under her eyes. Muscle tone less doughy than before, but she still had a tendency to melt in the examiner's lap. After an initial adjustment, she was outgoing and friendly. She thoroughly enjoyed the developmental examination, showed interest in exploiting all the materials, and responded quickly to directions, seeming eager to please. Quantitatively her speech and behavior were at a 36 month level except for an advanced visual-motor performance: she copied a cross, quickly placed all the color forms, and drew a "baby" with legs, feet and eye. However, her spontaneous productions showed a preoccupation with fearful fantasies. Her opening gambit was to point to a minute scratch on her finger, saying, "Man did it at night" with a knife. After correctly identifying a "mamma pig and two baby pigs" in a picture, she told of how a pig pulled her down on the grass, put something around her neck and pulled it tight.

V. showed only minor unevenness in her early development. From the beginning, she was extremely responsive to stimuli and is now outgoing and somewhat above average in development. However, she tended to have nighttime irritability from her first month and was quite anxious from around 24 to 30 months of age. She still is moderately preoccupied with fears of bodily harm, but this has not grossly interfered with her relationships. Her mother's anxiety undoubtedly contributed to V.'s insecurity, but this has been offset to some degree by the fact that the more stable father and grandmother care for her most of the time.

Three infants whose over-all development was normal as regards plasticity, each had isolated abnormal findings described briefly below.

Carol was the first baby born to an immigrant couple who eagerly looked forward to her arrival. Birth weight was 9 lb., 12 oz., and she continued to be a large, fat baby, whose body growth was rapid and who developed at an average rate in all other areas. In the first two months her muscle tone was soft, but her color,

activity and postural tone were good. Later she was so fat that it was difficult to evaluate tissue turgor, which still appeared to be somewhat soft. She was two months slow in standing and walking, apparently because of her weight. She was always a placid, friendly and contented child who resembled her mother in these respects as well as physically.

Grace was the first baby born to a 36-year-old woman who was widowed during her pregnancy, but who provided a stable, well-ordered home and took great pleasure in the baby. G.'s birth was prolonged and traumatic with delayed respiration. Birth weight 6 lb., 2 oz. She grew evenly, being physically petite and evenly advanced in all other areas. She had a transient rash following orange juice at one month, and developed allergic rhinitis at 6 months, following exposure to sprayed trees. This symptom became troublesome enough during her second and third winters to necessitate desensitization. At 11 and 13 months her muscle tone was soft, but there were no other signs of physiological instability. She was always alert and very active and social, taking great pleasure in her abilities in the first 1½ years. She spoke late in the second year and became rather shy in her third year, but had no unusual anxiety.

Wilma was the second baby born to an unmarried woman of limited intelligence. The first baby had died suddenly at one year of unknown cause. W.'s mother remained home on public assistance to care for W. and was affectionate and warmly accepting with her. W.'s birth weight was 9 lb. and she continued to be a large heavy baby with a large head. Development was even until seven months of age, when W. showed a decrease in the tone of her legs. From 7 to 17 months muscle tone was mushy. At one year locomotion lagged behind the rest of her development. She had four convulsions between 13 and 16 months of age; the first 3 were nonfebrile and investigation did not reveal the etiology. The last occurred during mumps. Her development proceeded normally thereafter. She was always an active, alert and friendly child.

IV. Discussion

Using Bender's criteria (8, 9), P., F., and C. were identified at the age of one month as being "vulnerable" because of abnormally uneven development that distinguished them from the other infants examined. All three had vasomotor instability; P. and F. had molluscous muscle tone. P. had most signs of immaturity. He was torporous, inactive and showed a slow-motion, writhing motility, reminiscent of Gesell's mid-fetal infant of 32–36 weeks gestation. In the presence of normal head and eye control, his trunk exhibited a startling lack of tone. F. was also hypoactive, but he was torporous for a shorter period; his motility was more mature and trunk tone was firmer. C's motility was similar to F.'s, but he was never noted to be torporous. P. was underresponsive to stimuli, while F. and C. were extremely responsive. V. also showed vasomotor instability and doughy tone at one month, but motility was normal and she was not identified as being vulnerable until her 4 months visit. At one month she showed increased responsiveness and was wakeful and irritable.

The subsequent development of P., F., and V. showed disturbances in all areas, biological and psychological, which conformed to Bender's description of the excessive plasticity in schizophrenic children. They showed disturbance of biological rhythms and tempos of maturation, and characteristically plastic organization of homeostasis, motility and perception, which had psychological repercussions in the areas of anxiety, body-image, identification, and reality-orientation. These later disturbances were profound in P., moderately severe in F., and relatively minor in V., showing the same order of severity as their initial immaturity. In P. and F. the disturbance in biological rhythms antedated signs of tension, and appeared to have a specific relationship to their later psychological problems and fluctuations in anxiety.

1. *Disturbance in the temporal organization of maturation*

All three infants showed unevenness in longitudinal development, with regressions, accelerations and retardation not observed in the other infants. This was seen most clearly when their development in all areas was graphed (figs. 1–4). The lags and spurts produced a chaotic step-like picture for P. and F., quite different from the even slopes of the other infants (fig. 4). V. showed this unevenness to a minor degree.

For example, P. could hold his head up in the prone and erect positions at 1 month, but was unable to lift it at 3½ months, and was barely able to lift it again at 6 months. He was unable to sit at all until 10½ months, but then stood up alone at 11½ months and walked with support at 13½ months. He said no words until 27 months, then spoke two to three word sentences by 29 months. V.'s head control was advanced at 1 month

and retarded at 4 months, when she also showed a marked regression in trunk control.

All three infants showed discrepancies between development in different areas at any one time, and even between different aspects of single functions. In the first year, eye-hand coordination and fine manipulation proceeded evenly, and showed all three infants to have at least average potential. However, postural control developed unevenly. It lagged briefly in F. at 7 months, when he was able to stand, yet unable to roll from the supine to the prone position. V. had difficulty in the control of the trunk only from 4 to 7 months of age. P.'s lag in control of his trunk was so marked between 1 and 9 months that at 9 months he had less control of his body than a normal 5 month old.

During the periods when they had poor postural tone these babies cried when in unsteady positions, and P. and F. were even helpless and miserable lying supine. At 7 to 8 months of age, P. tended to hold himself in stiff, awkward, hyperextension, with plantar-flexion of the toes, his arms outstretched with fingers curling and uncurling, whenever he was in unsteady positions, apparently in a vain attempt to increase postural tone and regain equilibrium. This stiffness made his reaching for objects appear jerky and awkward. He relaxed and was completely flaccid only when his whole body was cradled. V. briefly showed a much milder tendency to plantar flexion. At no time did P. or V. show any associated alteration of deep tendon reflexes.

Since development proceeded so disharmoniously, there were profound repercussions which are not seen in normally developing children, nor in those whose development is uniformly retarded. Because of the greater discrepancies in his development, these secondary problems were most prominent in P. P. was essentially attempting to master problems of manipulation and spatial relationships at a 7–9 months level with an organism which was still struggling with problems of postural station and equilibrium at a 4 month level. His inability to sit narrowed his horizon and limited his ability to explore his environment at the time when manual dexterity was nascent. This must have affected his picture of himself in relation to his world, since this depends upon the integration of visual, tactile and kinesthetic impressions. In P.'s development these areas were out of step, and all impressions were integrated in the context of marked anxiety in relation to gravity. He never showed the pleasure in activity and bodily movement nor the satisfaction in achieving manual dexterity that normal infants do until he achieved secure, independent walking. Just as his body image must have been distorted by his postural insecurity, so in a broader sense his developing ego must have been handicapped by his ineffectual attempts at mastery.

Like the brain-damaged child with similar problems (6), P. needed the physical support of an adult's body during this period of lagging postural control. He was most relaxed when cradled in the examiner's lap, and only when completely supported did he perform manual tasks optimally. However, his grandmother was emotionally incapable of responding to his need for special attention. The fact that he suddenly began to progress, despite the fact that he was still totally under her care, indicates that there must have been an abrupt change in his inner resources.

During his second year P. showed a completely different picture. From 13 months on his motor development was practically normal, and it soon far outstripped his lagging manipulative skill, and his language and social development. However, although motor development was quantitatively normal, it did not become organized into more mature behavior because of his uneven development. His maturing locomotion wasn't linked with developing manual skills, for broadening exploration of his physical world. Thus, locomotion was never integrated into useful service for the whole organism so that it could develop into more complex behavior. It remained movement for movement's sake, with a persistent qualitative immaturity in its lack of patterning.

2. *Disturbance in physical growth*

An unexpected finding was the degree to which unevenness in somatic growth paralleled the fluctuations in other aspects of development, although it is known that the Wetzel Grid reflects changes in the emotional

well-being of older children (17, 18). In P.'s first year and F.'s first two years body growth and head growth lagged and accelerated in proportion to the lags and accelerations in other areas of development, especially locomotion and language. This was more remarkable since in both children the accelerated growth occurred several times in the face of repeated respiratory infections and diarrhea. Unlike these two, V.'s lag in growth came after she had already recovered from the lag in postural tone, and in her the lag in growth coincided with a time of rapid neuro-muscular development. It appeared to be related to her severe respiratory illness during that period.

3. *Disturbance in vaso-vegetative functioning*

Vasomotor disturbances were prominent in these three children, including pallor, cyanosis and mottling of peripheral origin, and dermatographia. Similar phenomena were not observed in the other children studied. In general these changes became more severe during the periods of greatest developmental retardation.

V. had a sensitivity reaction to her first DPT injection and is believed to have a mild allergic component in her respiratory infections. Grace, one of the non-vulnerable infants also has an allergic history.

Spastic constipation, anorexia and sleep disturbances occurred more frequently over longer periods in P., F. and V. than in the other children studied, where they appeared only as sporadic phenomena. However, only P., at his lowest ebb at 9 months, was unable to suck and had to be fed with a spoon. P. at 9 months and V. from 4 to 7 months were spontaneously reported not to cry with hunger although they seemed ready to eat when fed after 5 to 6 hours. This suggested some alteration of gastric tone or a lack of awareness of inner stimuli; but the data on this are too scanty to draw any conclusions.

4. *Activity disturbance*

Unlike any of the other infants, both P. and F. showed prolonged torpor and hypoactivity at first that was reminiscent of Gesell's description of the fetal infant (26). F. slept continuously for the first week and had to be awakened for feedings. At five weeks of age he still frequently fell asleep after the first five minutes of nursing. Even when awake he moved very little. P. was even more inactive at five weeks than F. He lay still except for slow motion, fish-like movements and showed none of the usual brisk kicking. When prone, although he could lift his head, he did not work at it; he waved his legs but did not push.

By 11 weeks of age. F. was extremely active and continued to be so thereafter. P. continued to be underactive until 16–18 months of age when he walked securely, and for the first time seemed interested in moving about. Until then his activity was markedly diminished, and when he did move, he did so slowly, giving an appearance of caution or deliberation and showing a marked lack of vigor and drive. Even when he reached for objects, he looked for a long time before doing so. If something was moved out of reach, he remained impassive, neither reaching for it nor showing signs of frustration. He exploited objects much less than normal until 11 months, with little of the usual banging, waving, mouthing, etc., even though his manual dexterity and strength were quite adequate. It was as if he were unable to completely overcome the initial torpor, so that his activity throughout the first year was marked by a residual asthenia. What started as a physiological state, gave the appearance of passivity and a striking lack of interest and initiative when it continued into more patterned behavior.

5. *Specific motor disturbances*

All three children had molluscous muscle tone when first seen and with some fluctuations throughout their course. It was usually more prominent during the periods of greatest retardation. The soft tone seemed to be an intrinsic tissue tonus since it varied independently of any change in deep tendon reflexes.

F. has always shown an excessive physical compliance. P. melted in the examiner's lap for his first 15 months, but since 18 months he has appeared terrified and does not tolerate any physical contact except with his mother. All the other infants felt discrete when held as soon as they had achieved independent sitting.

The data were inconclusive concerning the persistence of tonic neck reflex behavior. This reflex is conspicuous in normal infants up to 3

months of age in their spontaneous postures, or when it is elicited by turning the head and it normally disappears by 5 months (27, pp. 301–302). It was unusually prominent in C. at 1 month, and was prominent in V. through 7 months of age and in P. through 6 months. However, it could not be elicited in F. after 3 months of age. Interestingly, of all the infants, F. is the only one who as a runabout has shown an unusual amount of whirling behavior in his spontaneous play. In the "non-vulnerable" infants, the tonic neck reflex was not elicited after 3 to 5 months of age.

The outstanding uneveness in the postural development of these 3 children in their first 7 to 9 months has been described above. It suggests temporary disruption of whatever central nervous system mechanisms ordinarily control the cephalo-caudad gradient and orderly progression in motor development

6. *Plastic organization of perceptual impressions, and disturbance of body image and orientation in space*

The data collected under this heading were only fragmentary, but suggestive. F. showed the most pronounced findings. At 4 months, although he focused on and followed objects in space, reached and grasped well for his age, he did not look at objects once they were in his hand. This lack of response to the proprioceptive stimulus is a primitive form of deficient self-awareness. P. was the only other infant who showed this discrepancy between the awareness of objects in space and those he held.

At nine months F. was "fascinated by people's feet". He had only just discovered that he could duck his head in order to creep under furniture, and he was precociously investigating the rear of the mirror after seeing his reflection. Unfortunately we cannot know what he expected to find there, but his confusion concerning boundaries and transparency was also seen from 13 to 15 months. He tried to drink from the bottom of a cup; he examined the underside of the paper on which he scribbled; he tried to reach and insert objects through glass and plastic containers.

I suspect it was a confusion about his own body boundaries, perhaps related to the earlier poor organization or awareness of proprioceptive impulses and confusion about boundaries in space which gave rise to his fear of his own feces at 13 months. This phenomenon appeared before training of any kind had been attempted, and it startled his mother. At 19–22 months these body fears were at a peak and were related to fears in spatial orientation. He was afraid of a toilet flushing, of a bath, even of being sponged with a cloth, and worried about where everything went: bath water, a ball disappearing and people who left. By this time his inner confusion had undoubtedly been compounded by his mother's increased anxiety and her inconsistent attempts at toilet training. A remnant of this early confusion appeared at 33 months in his calling his feces "pants" although he used "b.m." for dog's feces. His present struggle with identification is now inextricably bound up with his mother's own confusion and her difficulty in helping him to establish patterns or limits.

At three years of age Frank's superior performance with the formboard and matching color forms contrasted markedly with his difficulty in identification and poor imitation of another person's movements. This picture is reminiscent of what can be seen in an exaggerated form in autistic children, where it has been ascribed to the tenuous nature of object relationships, with a compensatory preoccupation with boundaries (29). In Frank's first months of life, one can see basic disturbances which could produce this picture. He showed a delay in the organization of proprioceptive impressions at 4 to 9 months, and an abnormal fluidity in the perception of boundaries in space, accompanied by a precocious preoccupation with such boundaries most marked from 9 to 15 months. These early perceptual disturbances would have produced an inadequate inner awareness of his own body in movement and in space which antedated, and appeared to be related to, the later more complex disturbances in identification and imitation of movement.

There was fragmentary evidence that P. had some similar difficulties in integrating perceptual experience. Because his perceptual symptoms were less marked than his outstanding motor difficulties and because the mothering care he received was so inadequate, it is more difficult to assess the importance of

these factors in P.'s later development, especially since he could not communicate verbally in the early period.

However, P. was the only baby besides F. whose hand-regard lagged behind his perception of objects in space. Interestingly, he seemed fascinated by his empty hand into the tenth month, long after he should have lost interest in it. One can only speculate whether this preoccupation was due to the delayed integration of proprioceptive impulses, or to a more general withdrawal of his interest from the environment at that time. Similarly at 31 months he attempted but was unable to imitate circular and vertical pencil strokes. However, he responded at his age level after his hand was guided in one movement. It appeared that he had insufficient awareness of his own body image to translate the visual picture of another person's performance into similar action by himself although he was capable of repeating the movement after he had experienced it passively. This suggests that he could have learned activities at home had he been given patient physical guidance, and his manipulative ability might not have lagged as it did after one year.

7. *Relationship of anxiety to disordered maturation*

Both P. and F. showed clear evidence of uneven maturation on their one month examination, two to three months before they showed any signs of tension, irritability or anxiety. The absence of irritability was not a function of being generally unresponsive, because F. was already excessively reactive to all environmental stimuli and had a precocious social smile. The fact that the biological disturbances appeared before anxiety provides important corroboration of Bender's concepts of the meaning of anxiety in schizophrenia and other disorders of childhood (7). In the subsequent months the fluctuations of irritability and anxiety in these two infants, as well as in V., frequently ran remarkably parallel to the disturbances in maturation. As the children grew older, this primary anxiety was overshadowed by the more complex problems of identifications and relationships.

P. began having night-time irritability at 3½ months, which became increasingly severe until 9½ months. This was the period in which postural tone and motor behavior lagged increasingly, followed by lags in other areas of development. During the period of rapid acceleration in motor behavior and bodily growth between 9½ and 13½ months, his irritability diminished. It disappeared by 11½ months.

F. had minor night-time irritability at 4 months, which became marked at 7 months, at the time his postural development was most retarded. From 9 months on his difficulties were largely in the area of perceptual confusion, identification, and relationships. His anxiety increased with the onset of these symptoms at 9 months, but then fluctuated inconsistently, except for the period of extreme fears between the ages of 18 and 22 months.

V.'s night-time irritability was present at one month and became marked at 4 months when her postural tone regressed. It began to subside at 8 months, when her motor behavior began to accelerate and disappeared by 13 months, after development was in balance.

These observations give the impression that in the early months of infancy irritability increased (or the threshhold for anxiety fell) *because* maturation was proceeding unevenly. Particularly the observations of uneven development in P. and F. before the onset of tension support this view, in contrast to the idea that extreme scatter in performance is the result, rather than the cause, of the anxiety or stress (14, 28).

8. *Predictive value of the early disorganization of maturation*

If the original theoretical premises are correct, then those infants who showed the most marked disturbance of maturation, as described above, should prove to be those infants most vulnerable to schizophrenia. This study demonstrates that it is certainly possible to distinguish some infants from their peers on the basis of these criteria. However, the ultimate fate of the "vulnerable" and "non-vulnerable" children will not be known for some years. Furthermore, a much larger series should be studied, to obtain a fuller picture of what can happen to such children in later life.

Keeping these limitations in mind, some provocative relationships emerge from an

examination of the preliminary observations. The vulnerable infants P., F., and V. all showed more profound variability in development than the other infants studied; the deviations being most marked in P. and least in V. These three infants shared several features which distinguish them from the rest of the group.

1) Disorganization of the normal temporal relationships of maturation. They deviated not in merely being slower or faster than the average, as did the non-vulnerable babies, but in having a constantly changing rate of development as compared to the average. Further, the rates of development of different functions did not bear a constant relationship to each other as they did in each of the non-vulnerable infants. The latter tended to have a constant profile of their functions throughout the study, e.g., W. was faster than average in body growth, average in adaptive language and social behavior, and slower than average in motor behavior. G. was far above average in motor skill, somewhat above average in adaptive and social behavior, only average in language and below average in body growth. In contrast, in the three vulnerable infants, the rate of the development of the different functions bore a constantly changing relationship to each other, so that the profile of the infants' capacities changed from one examination to the next.

2) A pan-disorganization of development. Three of the non-vulnerable infants showed uneven development of one function at some time in the study (W., G., C. above). In contrast to this, in the vulnerable infants there was no area of development, biological or psychological, that escaped disturbance.

3) Only the three vulnerable infants had persistent molluscous muscle tone and vasomotor disturbances.

4) P., F., and V. were also distinguished by their uneven motor development, with a temporary lag in postural control in their first 9 months of life. Of the non-vulnerable infants, W. was the only one who had any similar difficulty. However, her motor lag from 7 to 17 months was followed by convulsions and appeared to be part of an as yet undiagnosed neurological condition. This differed from the disturbance of P., F., and V. in that it was an isolated neuromuscular disorder of central origin that was unassociated with disturbances in other areas of development.

There also appeared to be significant differences that distinguish P. and F. from V.

1) In P.'s first year and F.'s first 2 years the lags and accelerations in other areas were accompanied by parallel lags and accelerations in body and cranial growth. V. showed no such positive correlation. She maintained her rate of physical growth while motor development lagged; and body and cranial growth dipped right after this, when motor development was again accelerating.

2) P. and F. had an initial period of torpor and hypoactivity in the neonatal period, whereas V. already showed excessive wakefulness and irritability in the first month.

3) Possibly related to 2), V. later showed sensitivity or allergic reactions.

Of all the infants P. was the only one who had a diminished responsiveness to stimuli. Possibly related to this, P. appeared to be of low average intellectual potential, while F. and V. were high average.

The personality disturbances of these children show a corresponding gradation in severity. In the first months of life and at 3 to 4 years of age the three vulnerable infants were distinguished from the other infants by a lower threshold for anxiety. V. who was identified as vulnerable at 4 months and whose developmental disturbance was quite mild has shown little anxiety compared to P. and F. and no signs of personality disorganization or regression. P. who was identified at one month as vulnerable and whose biological disturbances were the most severe initially and in the first year is now considered to be schizophrenic. The fact that P. was cared for by the sickest mother (and mother substitute) obviously contributed to his personality disorganization, but there are many features of his earliest months that cannot be explained on this basis alone. F.'s early developmental deviations and his present personality problems are of severity intermediate between those of P. and V. He is considered to be a disturbed child at this time, who has not been diagnosed as schizophrenic, but his ultimate prognosis is considered guarded.

Even from these preliminary observations,

it appears that it was possible, using physiological criteria, to identify as early as one month of age an infant who later developed schizophrenia. The fact that two infants with lesser developmental deviations show milder personality difficulties that are much more severe than anything seen in the babies with normal development, raises the broader question as to whether milder degrees of physiological vulnerability may also have significance in later personality disturbances.

9. *Comparison with other studies of infant development*

If the observations reported here have any objective validity, then one should find infants with features similar to P., F. and V. in earlier studies of infant development. This actually proves to be the case.

Gesell reported such infants under "Atypical and Pseudoatypical Growth Complexes" (see "U.V." in (25), Chapter 10) and under "Borderline Unstable" (see cases 2 and 4, pages 133–134 in (27)). This latter term connoted mild retardation "combined with impulsive, highly changeable and other atypical emotional reactions." Gesell included another case under "Pseudosymptomatic Retardation" (27, case 2, p. 139) to indicate that it was "in reality a true amentia of primary or secondary origin" which others falsely attributed to environmental causes or to emotional blocking, and so to emphasize that the bizarre, erratic behavior did not portend normal development in the future, despite the elusive aura of normality.

Of the 16 babies studied in detail by Shirley for more than 2 years (30, 31, 32) "none could be called a problem child." (32, p. 206). Indeed, none of the infants showed as extreme unevenness in development in their first year as did Peter. However, the two most irritable children in the group, "Virginia-Ruth" and "Maurice", showed some early delay in language development. Virginia-Ruth, who was persistently negative and antisocial, was slow in language development between 4 and 12 months of age (31, p. 407) and later "much of her speech was egocentric." (32, p. 143). Maurice did not talk until 3 years of age (32, p. 182). Neither child appears to have had any marked lag in postural development, sufficient to show up in the quantitative scores (30, pp. 212–214), but both had low total scores in the first 2 years attributed to irritability, negativism and boredom (32, pp. 100–103). However, from her detailed study of these milder personality variations, Shirley concluded that "differences in personality were apparent in some babies at birth and in all within the first 3 months. The traits change somewhat with age and experience, but always in ways that seem compatible with the original personality nucleus." (32, p. 207). She concluded that tendencies toward good coordination and strong motor drive (30, p. 194) and to irritability (32 p. 40) were probably inborn.

Bayley reported two infants with slow postural development and a "low I.Q." around 6–7 months, who later tested very high (I.Q.'s 170 and 189) in verbal abilities (3). She did not attempt to explain the unevenness, but merely cited these cases to point out that "I.Q." in infancy and I.Q. after two years of age are measures of two different functions (e.g., sensori-motor, and verbal ability) (1, 2, 3).

Certain studies have gone further than this and have attempted to correlate specific aspects of early development with the later development of personality deviations, and especially with childhood psychosis. Naturally, the emphasis in each instance has varied according to the observers previous experience and theoretical background. However, one finds striking similarities between the infants who have been subjected to the various interpretations.

Fries found that infants examined in the first ten days of life showed fundamental differences in their "congenital activity pattern", as gauged by their over-all activity-level, startle response, and reaction to oral frustration (19, 20, 21, 22). She believed that at that age, environmental factors were at a minimum, and the activity pattern was probably determined primarily by the excitability of the neuromuscular system (21). However, her follow-up studies showed "no one to one correlations between activity type and later personality." "No child developed a psychosis in childhood or adult life," but Fries speculated that Kanner's Infantile Autistism probably developed in an extremely pathologically

"quiet type", and might be detected at birth (23, 24). She believed that the quiet type would tend to achieve mastery through a symbiotic relation with the mother, and therefore the activity pattern could account for any increased sensitivity to the mother's affect.

Escalona reported a number of children who later developed "childhood psychosis which is closest to Kanners early infantile autism" whom she found had a lowered threshold to stimuli (12). This apeared to be a constitutional increase in sensitivity, with a decreased tolerance to the ordinary stresses of life (12, 28),which made the children "unable to interact with a normal mother" (16). She "speculates that the excessive tension so induced may interfere with the orderly integration of functioning." According to this view, the uneven development with abnormal scatter in developmental tests is secondary to the unusual stress (28). However, the data given on one of these infants ("Tommy", or "Bruce"), observed from the age of 12 weeks, show that in addition to this increased sensitivity and heightened perceptual discrimination, he also had other deviations in the early months similar to those described in detail above for Peter, Frank and Vera, namely: vasomotor instability, a period of no weight gain despite an enormous appetite, poor tone, underactivity, delay between perception and response, retarded motor development, and development characterized by a lack of "pleasure from increased control over his body" (12, 15).

From the Yale study Wolf has reported a child ("Christina") (34, 35) like Fries' "quiet types" and Escalona's excessively anxious infants, whose equipment made "observing more important than mastery." Christina had increased perceptual sensitivity and little motor drive. Wolf described the interaction between Christina's innate tendencies and her mother's need for an exclusive relationship. In the interpretation, however, more emphasis is placed on the latter. The data reveal a marked postural lag, but the child's hesitation to reach out for objects at 9 months of age was attributed to the mother's need to hold on to her. One wonders about the opposite possibility that Christina's unstable equilibrium may have contributed to her hesitation and could even have made the mother herself inclined to hold Christina more firmly. Another of the infants ("D"), reported by Coleman, Kris and Provence (13) from this same group, apparently developed very unevenly. Trunk and gross motor control lagged behind fine coordination, and the infant could not sit up by 8 months of age. However, they explain the subsequent spurt in maturation by the change in the mother's attitude and the increased participation by the father, "interacting with the forces of maturation."

Comparison of these reports makes it apparent that similar infants have been studied from several points of view. The initial torpor seen in Peter and Frank at one month recalls Fries' excessively "quiet" babies, such as "Anna" (20) and "Kate" (23). Both Peter and Frank have several features seen in Escalona's "Tommy" (or "Bruce") and Wolf's "Christina".

The above studies have emphasized 1) innate activity drive, 2) innate perceptual sensitivity, or 3) parental interaction with the innate pattern of the infant as being etiological in later personality formation. The author believes that by applying Bender's more holistic concepts to the study of very young infants it is possible to bring together the observations made both here and by these authors in a more meaningful way.

10. *Implications for further research*

1) That it was possible to detect an infant who later became schizophrenic, by applying Bender's criteria to a random sample of infants, provides direct corroboration of her concept that the schizophrenic child is distinguished at an early age from his non-schizophrenic peers by specific biologic signs of disordered maturation. Furthermore, this infant's later development illustrated the features predicted by Bender, namely, a) overall plastic patterning of development in all areas; b) immature homeostasis; c) early torporous state; d) molluscous muscle tone; and e) immature posture and motor activity.

2) From a practical standpoint, Bender's physiological criteria, as applied to the present pilot study, demonstrated their usefulness as a means of screening "vulnerable" from "nonvulnerable" infants. A much larger study with

longer follow-up is planned to determine the ultimate fate of such vulnerable and non-vulnerable infants, and so to determine what factors are specific in prognosticating later development (e.g., timing, duration, severity of deviations, etc.). Such a study could determine with more statistical validity how the fate of such infants is influenced by environmental and other stress. It would be of utmost importance to study how the outcome can be influenced by creating a more favorable environment for such children and what can be done to treat the early physiologic symptoms before these distort the developing personality.

3) The existence of identifiable physiological differences between the schizophrenic infant and other infants at one month of age indicates that there is indeed a biological predisposition to schizophrenia, and this was found to be present before anxiety or personality symptoms as such were manifest. Some of the profound repercussions of the biologic disturbance on the developing personality were observed directly, but only a beginning was made in this direction in the pilot study.

The essence of the biological disturbance appeared to be in the faulty timing and integration of all aspects of development, including physical growth, homeostatic control, neuromuscular development and perceptual organization. The material suggests that further investigation into the underlying physiologic disturbances in schizophrenic infants, provisionally identified by some such criteria as used here, should focus on the mechanisms which regulate the gradient, temporal pattern and total integration of development. The association in Peter and Frank at one month of age of extreme somnolence and of torpor, even when awake, with the vasomotor and other disturbances, suggests that the relation of hypothalamic function to the initial disorder deserves attention.

BIBLIOGRAPHY

1. Bayley, N.: Mental growth during the first three years. *Genetic Psychology Monographs, 1:* 1–92, 1933.
2. Bayley, N.: Consistency and variability in the growth of intelligence from birth to eighteen years. *J. Genet. Psychol., 75:* 165–196, 1949.
3. Bayley, N.: Normal growth and development. In *Psychopathology of Childhood.* Ed. by P. Hoch and J. Zubin. New York: Grune & Stratton, 1955, pp. 1–14.
4. Bender, L.: Childhood schizophrenia. *Nerv. Child, 1:* 138, 1942.
5. Bender, L.: Childhood schizophrenia. *Am. J. Orthopsychiat., 17:* 40–56, 1947.
6. Bender, L.: The psychology of the brain-damaged child. *Am. J. Orthopsychiat., 19:* 404–415, 1949.
7. Bender, L.: Anxiety in disturbed children. In *Anxiety, A Symposium,* Chapter 7. Ed. by P. Hoch. New York: Grune & Stratton, 1950, p. 119.
8. Bender, L., and Freedman, A. M.: A study of the first three years in the maturation of schizophrenic children. *Quart. J. Child Behavior, 1:* 245–272, 1952.
9. Bender, L., and Helme, W. H.: Quantitative test of theory and diagnostic indicators of childhood schizophrenia. *Arch. Neurol. & Psychiat., 70:* 413, 1953.
10. Bender, L.: Treatment of juvenile schizophrenia. In *Neurology and Psychiatry in Childhood.* Baltimore: The Williams & Wilkins Co., 1956, 462–477.
11. Bender, L.: Longitudinal study of ninety schizophrenic women. Paper presented at the Meeting of the Society for Biological Psychiatry in Chicago, April 28, 1956.
12. Bergman, P., and Escalona, S.: Unusual sensitivities in very young children. In *The Psychoanalytic Study of the Child.* Vol. III/IV. New York: International Univ. Press, 1949, pp. 333–352.
13. Coleman, R. W., Kris, E., and Provence, S.: The study of variations of early parental attitudes. A preliminary report. In *The Psychoanalytic Study of the Child,* Vol. VIII. New York: International Univ. Press, 1953, pp. 20–47.
14. Escalona, S.: The use of infant tests for predictive purposes. *Bull. Menninger Clin., 14:* 117–128, 1950.
15. Escalona, S.: Paper presented at the Meeting of the American Psychoanalytic Association in New York, December, 1951.
16. Escalona, S.: Emotional development in the first year. In *Transactions of the Sixth Conference on Problems of Infancy and Childhood.* Ed. M. Senn. New York: Josiah Macy Jr. Foundation, 1953, pp. 11–92.
17. Fried, R., and Mayer, M.: Socio-emotional factors accounting for growth failure in children living in an institution. *J. Pediat., 33:* 444–456, 1948.
18. Fried, R., and Mayer, M.: Grid technique as tool for improving health services to institutionalized children. *J. A. M. A., 161:* 1–5, 1956.
19. Fries, M. E.: Factors in character development, neuroses, psychoses, and delinquency. *Am. J. Orthopsychiat., 7:* 142–181, 1937.
20. Fries, M. E., and Lewi, B.: Interrelated factors in development. *Am. J. Orthopsychiat., 8:* 726–752, 1938.
21. Fries, M. E.: Psychosomatic relationships between mother and infant. *Psychsom. Med., 6:* 159, 1944.
22. Fries, M. E.: Diagnosing the child's adjustment through age-level tests. *Psychoanal. Rev., 34:* 1–31, 1947.
23. Fries, M. E., and Woolf, P. J.: Some hypotheses on the role of the congenital activity type in personality development. In *The Psychoanalytic Study of the Child,* Vol. VIII. New York: International Univ. Press, 1953, pp. 48–62.
24. Fries, M. E.: In *Transactions of the Sixth Conference on Problems of Infancy and Childhood.* Ed. M.

Senn. New York: Josiah Macy Jr. Foundation, 1953, p. 83.
25. Gesell, A.: *Infancy and Human Growth.* New York: Macmillan, 1928.
26. Gesell, A.: *Embryology of Behavior.* New York: Harper & Bros., 1945.
27. Gesell, A.: *Developmental Diagnosis,* 2nd Ed. New York: Paul B. Hoeber, Inc., 1947.
28. Leitch, M., and Escalona, S.: The reaction of infants to stress. In *The Psychoanalytic Study of the Child,* Vol. III/IV. New York: International Univ. Press, 1949, pp. 121–140.
29. Ritvo, S., and Provence, S.: Form perception and imitation in some autistic children: Diagnostic findings and their contextual interpretation. In *The Psychoanalytic Study of the Child.* Vol. VIII. New York: International Univ. Press, 1953, pp. 155–161.
30. Shirley, M. M.: Postural and locomotor development. In *The First Two Years,* Vol. I. Minneapolis: University of Minnesota Press, 1931.
31. Shirley, M. M.: Intellectual development. In *The First Two Years,* Vol. II Minneapolis: University of Minnesota Press, 1933.
32. Shirley, M. M.: Personality manifestations. In *The First Two Years,* Vol. III. Minneapolis: University of Minnesota Press, 1933.
33. Wetzel, N. C.: The baby grid. *J. Pediat., 29:* 430–454, 1946.
34. Wolf, K. M.: Observation of individual tendencies in the first year of life. In *Transactions of the Sixth Conference on Problems of Infancy and Childhood.* Ed. M. Senn. New York: Josiah Macy Jr. Foundation, 1953, pp. 97–137.
35. Wolf, K. M.: Observation of individual tendencies in the second year of life. In *Transactions of the Seventh Conference on Problems of Infancy and Childhood.* Ed. M. Senn. New York: Josiah Macy Jr. Foundation, 1954, pp. 121–140.

106 East 85th Street
New York, N. Y.

CHLORPROMAZINE THERAPY IN PRIVATE PRACTICE

Its Benefits and Complications

STANLEY LESSE, M.D., SIDNEY MALITZ, M.D., AND PAUL HOCH, M.D.[1]

Three and a half years have passed since chlorpromazine, then known by the research code number 4560RP, was reported as being efficacious in psychiatric problems (6, 7, 8, 9, 15, 16). Since then hundreds of articles have appeared in the literature on its use. Almost all of the papers reporting on statistically significant numbers of patients have come from large state hospitals. Some of these reports have been very glowing as to the results of chlorpromazine therapy and have inferred that this mode of treatment has made the use of other organic therapies such as electroshock, insulin coma and psychosurgery almost obsolete (19, 25, 27).

State hospital mental patients form a very specialized segment in the psychiatric realm, for they represent those patients who frequently have been ill for a long period of time, and are often very agitated, who frequently have evidences of deterioration or dementia and who have been isolated, often for years, from the responsibilities of everyday life. The efficacy of chlorpromazine therapy, in this group, is based on the degree of symptomatic improvement and the manageability of the patient on the wards. Improvement is considered as being very good when a patient is deemed ready for discharge. Benefits such as these are of extreme importance, but they must be supplemented to be made applicable to the wide spectrum of neuropsychiatric patients seen in private practice. These patients, in general, have been ill for a briefer period of time and are usually not as sick as those described above. Any criteria for improvement in this group must include an evaluation of their routine vocational and social performance as well as the degree of symptomatic remission.

In this paper we would like to present our findings in the use of chlorpromazine in routine private practice gathered over a one and a half year period with an evaluation of its benefits and its complications. On the basis of these findings we would like to submit criteria for the indications and contraindications of this drug in private psychiatric practice.

Methodology

Our case material consists of 199 patients. Seventy-three of these were males whose ages ranged from 15 to 80 years, while 126 were females 18 to 77 years of age. The patients diagnostically covered a very broad scope of psychiatric illnesses commonly seen in active neuropsychiatric practices. Broadly categorized 42 patients had psychoneuroses of various subtypes, while 157 had more malignant psychiatric ailments namely: a) 101 patients were diagnosed as having schizophrenia of various subtypes, b) 47 were classified as involutional psychoses (agitated depressions), and c) 9 had organic mental syndromes of different etiologies.

We would like to indicate that there are a small number of patients whom we have diagnosed as having early schizophrenia, who might be classified by some as having psychoneurotic illnesses. These cases fall mainly in the pseudoneurotic schizophrenic group. They were diagnosed as such after careful evaluation both from the longitudinal aspects of the history and the current clinical picture. All were found to satisfy the diagnostic criteria as set down by Hoch and Polatin (17, 26). We would also like to indicate that a few patients between the ages of 40 and 65, whom we have classified in the schizophrenic group, might be diagnosed by others as belonging to the group of involutional depressions. However, careful scrutiny of their past behavior revealed pronounced long-standing schizoid behavior. This fact plus the bizarreness of the symptoms during the present illness determined our placing them in that group of schizophrenic patients who have had a psychotic break in the involutional period of life.

[1] From the Neurological Institute of the Presbyterian Hospital of New York and the New York State Psychiatric Institute, New York, N. Y.

The duration of illness in our patients prior to their first visits ranged from 18 hours to more than 10 years, the vast majority having had marked difficulties for 3 weeks to 6 months. Forty-two had had previous psychiatric illnesses requiring one or more brief periods of private hospitalization. All patients included in this series, except those in whom the drug had to be stopped because of severe side reactions, were treated with chlorpromazine for more than a month.

Method of Evaluating Level of Improvement

Subjective and objective factors were considered. We attempted to quantitate these factors wherever possible, fully realizing the difficulties in evaluating the objective aspects of emotional illness let alone the subjective aspects. It will be noted that the criteria used stress the patient's adaptation to routine responsibilities of everyday life in addition to the degree of symptomatic improvement. Also the degree of pride and pleasure gained from successful performance was considered. In detail the factors evaluated were as follows:

I. *Performance*

A. Vocational performance

1. Excellent—full time employment. Functioning efficiently *without* strain. Great pride and pleasure from attainments.
2. Good—full time employment. Greater effort required than was necessary prior to illness. Moderate pride and pleasure from attainments.
3. Fair—working intermittently with considerable difficulties, frequent absences. Faulty performance at times. Lack of pride and pleasure.
4. Poor—unable to perform at all.

B. Social performance (individual and group interpersonal relationships)

1. Excellent—active and comfortable. High level of pride and pleasure obtained.
2. Good—active but with slight to moderate difficulty at times. Limited pleasure capacity.
3. Fair—socializes with great difficulty. Readily becomes very anxious. Lack of pride and very limited and infrequent pleasure.
4. Poor—seclusiveness and chaotic relations.

II. *Amelioration of anxiety*

Anxiety is defined for our purposes *here*, in its broadest aspect. We will consider it synonymous with fear whether this fear is generated by unconscious conflict or actual environmental difficulties. We attempted to quantitate anxiety according to a four-point scale after breaking down these psychophysiological phenomena into several components, namely 1) motor component, 2) affectual component and 3) verbal component.

1. Calm—no restlessness. Overt expression of fear, when it occurs, is appropriate to the severity of the actual stress.
2. Slight restlessness, slight affectual expression of fear, slight pressure of speech.
3. Marked restlessness, pacing. Marked overt affectual expression of fear. Often severe pressure of speech.
4. Panic.

III. *Amelioration of initial symptoms*

1. Excellent—all symptoms completely gone.
2. Good—symptoms markedly reduced in intensity and frequency. Patient able to cope with them.
3. Fair—slight improvement only, with the symptoms continuing to plague patient most of the time and with marked impact.
4. Poor—symptoms unchanged.

IV. *Dreams*

Whenever possible, dreams were sought out and studied in an attempt to gain additional information. Disappearance of nightmares, decrease in the frequency of rage dreams and an increase in the frequency of pleasant dreams were points that were evaluated.

The *final Improvement Rating* was indicated on a four-point scale which took into account all of the factors described above.

1. Excellent—full time employment. Active and comfortable in social performance. Marked pride and pleasure from vocational and social performance.

II. Good—full time employment but requiring slightly greater effort than usual. Active socially but with slight to moderate difficulties at times. Slight residual anxiety. Symptoms markedly reduced in intensity and frequency. Limited pride and pleasure from performance.

III. Fair—working but with considerable difficulties. Frequent absences. Socializing with great difficulty. Moderate to marked residual anxiety. Slight improvement in symptoms. Minimal pride and pleasure from performance.

IV. Poor—unable to perform vocationally or socially. Anxiety level severe and unchanged. Symptoms unchanged. Absence of pride or pleasure from performance.

Before presenting our therapeutic results, we want to give an idea of the degree of illness seen in our patients at the time chlorpromazine was started. Of the 199 patients being presented here, 170 were very ill, unable to perform vocationally or socially. They were dominated by their symptoms and in general were almost completely ineffectual. The remaining 29 patients were able to function with moderate to marked difficulties in either the vocational or social spheres but were severely handicapped by their symptoms. Those patients who were not as sick as the 199 considered here were not started on chlorpromazine at all but rather were managed with psychotherapy alone.

Evaluation of Therapeutic Results with Chlorpromazine

1) *Over-all improvement.* Of the 199 patients evaluated statistically, only 7 (4%) could be considered as demonstrating an Improvement Rating of I, while 41 patients (20%) showed an Improvement Rating of II. We may say, then, that approximately ¼ of all our patients have had very good results with chlorpromazine therapy and could return to satisfactory vocational and social performance. Seventy-one patients (36%) showed slight improvement (Improvement Rating III). The remaining 80 patients (40%) were not significantly helped in any way. This is shown graphically in figure 1.

2) *Age and sex as factors effecting degree of improvement.* The age and sex of the patients did not appear significantly to effect the improvement rating. We should state, however, that our figures may not be taken as being valid for children as we have had no experience with the use of chlorpromazine in pediatric patients.

3) *Degree of anxiety as a factor effecting degree of improvement.* Figures 2 and 3 reveal the important relationship between the degree of overt anxiety and the degree of improvement. It may be expressed in this fashion: The greater the degree of overt anxiety, the greater the

Fig. 1. Overall improvement with Chlorpromazine

improvement; the less the degree of overt anxiety, the poorer the results. Of the 48 patients having Improvement Ratings I and II (excellent and good), only four had an initial anxiety level of 1 or 2 (very little or no overt anxiety). Expressed in another way (shown most graphically in figure 3), only 4% of the 66 patients whose initial overt anxiety was nil or slight (anxiety levels 1 and 2) had excellent or good improvement ratings (Improvement Ratings I and II). This is in striking contrast to the fact that 34% of the 133 patients whose initial anxiety levels were severe or very severe (anxiety levels 3 and 4) attained excellent or very good improvement (Improvement Ratings I and II). On the other end of the improvement scale, we found that 64% of the patients with slight or negligible *overt* expression of anxiety showed no improvement (Improvement Rating IV), while only 28% of those whose initial anxiety was severe demonstrated a lack of improvement (Improvement Rating IV).

4) *Diagnosis as a factor effecting degree of improvement.* Figure 4 shows the relative degrees of improvement listed according to the general classes of diagnosis. In general, the percentage of patients having Improvement Ratings of I and II (excellent or good) was approximately the same in spite of the diagnosis (we have not included the organic psychoses in this statistical evaluation since the sample is too small). When this group was evaluated further, it was found that all but one had

DEGREE OF ANXIETY	IMPROVEMENT RATINGS I	II	III	IV
1	0	0	4	14
2	0	3	16	29
3	7	25	35	31
4	0	13	16	6
TOTALS	7	41	71	80

FIG. 2. Anxiety as a factor effecting degree of improvement

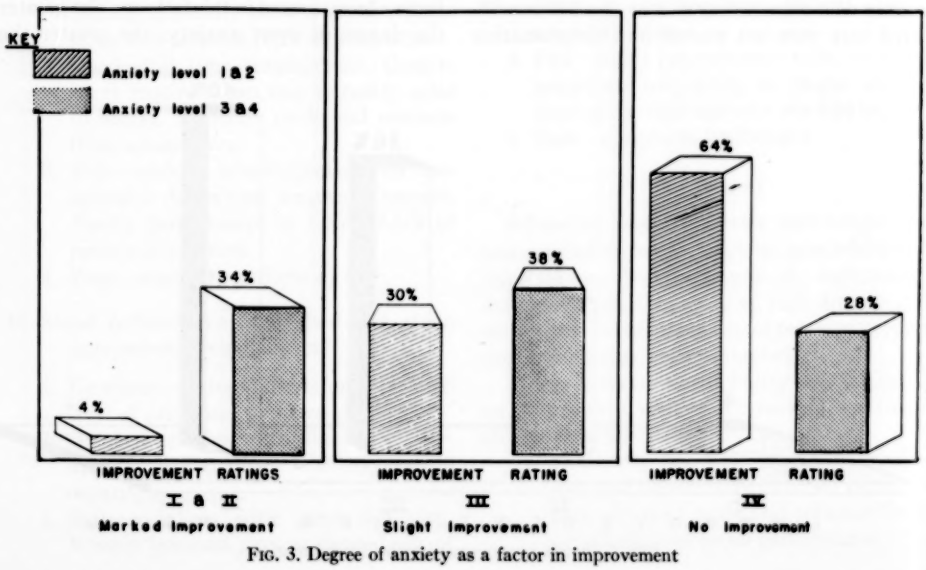


FIG. 3. Degree of anxiety as a factor in improvement

	IMPROVEMENT RATINGS			
	I	II	III	IV
SCHIZOPHRENIA				
Overt	4	12	18	31
Pseudoneurotic	0	6	13	17
AGITATED DEPRESSION	2	11	17	17
PSYCHONEUROSIS				
Anxiety States	1	7	2	1
Mixed	0	5	14	12

FIG. 4. Diagnosis as a factor effecting improvement

demonstrated marked or extremely marked overt anxiety prior to the onset of chlorpromazine therapy. Among the schizophrenic patients, those demonstrating marked anxiety were the pseudoneurotic or mixed subtypes, and it was among these subtypes that the best results were noted.

Among the patients diagnosed as having psychoneuroses, it was also those who had the greatest degree of anxiety who had the best results. Of those who had well-developed hysterical conversion mechanisms, with a belle indifference, none showed any significant improvement.

5) *Duration of illness as a factor effecting improvement.* As with psychotherapy and the organic therapies, the briefer the illness, the better are the therapeutic results. We found that those who had been actively ill for less than three months had the best results. Those who had been actively ill for more than six months had poorer results. There were several very striking exceptions to these rules, however. We have treated three schizophrenic patients who had been actively ill for 8 years or more, who had been through all of the accepted therapies, including psychoanalysis, electroshock, insulin coma, and in 2 cases psychosurgery, who have maintained an improvement rating of I and II for over six months on chlorpromazine.

6) *Dosages and rate of improvement.* Our initial daily dose varied from 50 mg. to 400 mg. The average was 100 mg. The initial daily dose depended on the severity of the anxiety. If anxiety was very severe, the drug was given during the first few days, either intramuscularly or intravenously, either alone or, if the patient would cooperate, in combination with oral preparations. We have given as much as 400 mg. intramuscularly during the first 24 hours in divided doses ranging from 50 to 100 mg. per injection. Our intravenous injections have ranged from 25 mg. to 100 mg., the latter amount given over a 30-minute period. When the medication is significantly efficacious, that given by the intravenous route works within 5 minutes and that given by the intramuscular route in from 10 to 30 minutes.

Our maximal daily dose with patients seen in office practice was 900 mg. per day. If the patient was hospitalized, it was carried to as high as 2,400 mg. per day. We found, with only 4 exceptions, that if the patient showed no significant response by the time we had gone up to 600 mg. per day, he obtained no signficant long-standing improvement though the dosage was elevated to over 1,000 mg. per day. If, on the other hand, there were significant

signs of improvement before the patient received 600 mg. per day, the dose was then raised until maximal gain was obtained. It should be mentioned that a few patients did not show their greatest improvement until the drug was lowered from the maximal dosage to 400 mg. or less per day.

Those who eventually demonstrated significant improvement began to show signs of this improvement during the first two weeks of therapy. If they did not, there was seldom evidence that prolonged therapy even in the range of 800 mg. per day or more would produce any significant lasting results. However, there were some who presented signs of slight improvement during the first two weeks who improved further after a longer trial.

Most patients who demonstrated the best results had to be given at least 400 mg. per day early in the course of treatment. There are, however, a few patients who have shown good responses with as low as 150 mg. Our technique is to maintain the maximal daily dose for at least two weeks. This is providing the patient shows a significant improvement. If the patient is not troubled by any side effects of the drug, the dose is left at its maximal level until there is definite evidence, from psychotherapeutic interviews and from reports of his vocational and social functioning, that he has shown and maintained satisfactory improvement. This period may be as long as six months, depending upon the degree of improvement. We would like to point out, however, that there is still no one established method to determine how long a given patient will have to be maintained on the drug.

The first indication of improvement is a decrease in the overt manifestation of anxiety. This is usually expressed as a decrease in the motor and affectual components of anxiety. This usually precedes the improvement in other symptoms.

7) *Duration of improvement.* Of the 199 patients being analyzed here, 129 have been followed for from 6 to 18 months. The others have been under treatment for not less than 3 months.

Twenty-eight of the patients who had shown improvement while on chlorpromazine had a complete exacerbation of their clinical syndromes. All but 9 of the patients who reverted back to the original state of illness did so during the first 3 months of treatment. The other 9 exacerbated after 6 months of therapy. In each case, the downhill trend was heralded by a gradual increase in anxiety followed by the return of the various abnormal clinical syndromes. Many of the patients who had shown improvement on the drug had episodes where they presented slight to moderate exacerbations of anxiety with an associated return of symptoms, but these were managed by psychotherapy, by increasing the dose of chlorpromazine, or by means of a combination of both techniques.

8) *Chlorpromazine and electroshock therapy.* A total of 60 patients who showed slight or no significant improvement (groups III and IV), after receiving what we considered to be an adequate course of chlorpromazine, were treated with electroshock therapy. Thirty-one patients had schizophrenia while 29 were classified as having agitated depressions. Thirty-six of the 60 patients, in whom chlorpromazine therapy had been unsatisfactory, demonstrated marked improvement after electroshock therapy and could be reclassified as having improvement ratings of I and II. All but 3 of these 36 patients, who demonstrated further improvement on electroshock therapy, were among those who evidenced marked anxiety.

On the other hand, there were 8 patients who had had only transient improvement from previous electroshock therapy who responded very well to chlorpromazine.

We have tried chlorpromazine in combination with electroshock on many occasions, but we have not found that the combined therapy decreased the number of shock treatments required for good results. At this time the entire question of combined therapy is controversial with regard to its efficacy and safety.

9) *Chlorpromazine and psychotherapy.* The general subject of the use of the ataraxics in combination with psychotherapy is one of the most provocative problems in present day psychiatry. Our observations, as far as we have gone during the past one and a half years, will be presented in detail in the near future. We would simply like to state here that chlorpromazine can at times serve as a convenient and beneficial adjunct in various psychotherapeutic

situations. There are some patients who are good candidates for psychoanalytically oriented psychotherapy in whom weeks or months might be spent by the therapist before the level of anxiety is decreased to the point where the patient is capable of cooperating in the mutual relationship that is fundamental for successful dynamically oriented psychotherapy. Chlorpromazine can, in certain cases, perform this task in a much shorter period of time. It can be used also during the course of psychotherapy if the patient becomes very panicky, while working through a problem, and the degree of anxiety becomes so great that it poses a threat to the continuation of treatment. When chlorpromazine is effective, it gives us an additional tool by which we can be of further aid to some of our patients undergoing psychotherapy.

In another paper one of the authors has presented the effects of combined therapy on the transference relationship, on the process of free association, on the unconscious meaning of the drug therapy itself, on dream production and on the patient's reactions to adverse side effects of chlorpromazine (23).

The Complications of Chloropromazine Therapy

Of the 199 patients in this survey, over 50% had some adverse effect from the use of the drug (figure 5). In many instances these adverse effects were very mild and transient and spontaneously cleared without the necessity of decreasing or stopping the drug. There was an even larger number of patients, however, in whom the severity of the side effects was annoying and which threatened to become more marked if remedial measures were not taken. For example, 44 patients manifested enough drowsiness to require the antidotal effect of some amphetamine preparation. Nose drops were often used to manage annoying nasal stuffiness, while mild analgesics were usually sufficient to relieve rheumatic complaints.

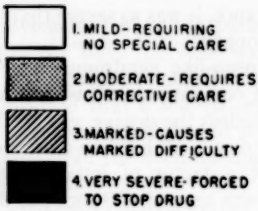
A total of 30 patients suffered from local or rather generalized pruritis. At times this was very annoying in spite of antihistamine drugs and analgesic ointments. In 11 cases a maculopapular rash was noted often involving all body areas. Marked sensitivity to heat and particularly to sunlight was seen in 8 cases. In one instance, it was so severe that the drug had to be stopped.

Parkinson-like syndromes were seen in 12 (6%) of our patients. This syndrome did not appear unless the dosage was greater than 400 mg. per day in all but one case, and in general was not a factor of importance unless the dosage was around 600 mg. per day or more. Usually, this symptom gradually disappeared as the dose was decreased, completely disappearing when the dose went below 300 mg. per day. The frequency of the Parkinson-like syndrome has been reported in as high as 10.9% of the patients (13), but this figure is much higher than those reported by most others. The cause of this syndrome has not yet been established but one recent report suggests that it may be due to alterations in copper metabolism such as is seen in hepato-lenticular degeneration (3).

Jaundice was a very disturbing complication in 7 (4%) of our patients. When present, it was very obvious. In 3 patients it was unaccompanied by any other symptoms, but in four there was fever, malaise, pruritis, nausea and vomiting and marked lethargy. The drug was stopped in all cases in which this complication appeared. In 5 patients the jaundice cleared within 3 to 4 days, but 2 others had residual signs for as long as 3 weeks. Surveys of over 10,000 patients (10) have revealed that the incidence of jaundice was 0.8–1.4% and that it almost always appeared during the second or third week of therapy, that it was mild and readily cleared when the drug was withdrawn. Our findings concur with these last two points.

We have not seen agranulocytosis in any patient in private practice although 75 were followed very closely with blood counts. A recent report (4) records 45 such cases from an estimated group of 4,000,000 patients who have received the drug. It was further estimated that the rate of incidence was one in 50,000–100,000 treated patients. One wonders whether the number of patients with agranulocytosis does not closely approach that seen in the general population in the absence of chlorpromazine.

In 17 patients with the diagnosis of schizophrenia, there was definite aggravation of the clinical picture. These manifestations included feelings of disassociation, feelings of deperson-


1. MILD - REQUIRING NO SPECIAL CARE
2 MODERATE - REQUIRES CORRECTIVE CARE
3. MARKED - CAUSES MARKED DIFFICULTY
4. VERY SEVERE - FORCED TO STOP DRUG

	1	2	3	4	Total
DROWSINESS	4	34	10	1	49
NASAL CONGESTION	16	17	0	0	33
DRYNESS	20	10	1	0	31
PRURITIS	6	4	8	1	19
AGGRAVATION OF PSYCHOSES	0	5	6	6	17
BULEMIA	8	7	1	0	16
GRIPPE-LIKE PATTERN	0	3	5	6	14
FATIGUE	0	9	4	0	13
ANOREXIA	4	5	4	0	13
PARKINSON-LIKE PATTERN	4	4	3	1	12
DERMATITIS	2	3	4	2	11
RHEUMATIC PAINS	1	6	2	0	9
CONSTIPATION	0	6	3	0	9
DIARRHEA	7	2	0	0	9
EDEMA	0	3	4	1	8
SENSITIVITY TO HEAT	0	2	5	1	8
JAUNDICE	0	0	2	5	7
NAUSEA AND VOMITING	3	2	0	0	5
HEADACHES (aggravated)	0	0	0	1	1

FIG. 5. Complications of Chlorpromazine therapy

alization, increased depression, increased restlessness. These symptoms occurred usually in those patients who felt peculiar and out of contact when they became drowsy. In 4, the drowsiness produced by the chlorpromazine was enough to precipitate severe psychotic patterns.

Depressed patients receiving chlorpromazine should be observed carefully, and close supervision is advised. We have seen 5 patients referred to us for electroshock therapy who have histories of suicidal attempts while taking the drug.

In a few cases, particularly during the first few weeks of therapy patients appeared clinically worse on the drug. Analyzing these patients further it was found that they had difficulty with reality contact when under mild sedation. This caused a paradoxical increase in anxiety. As one patient explained, "I feel

calmer in one way but I can't think as clearly, and it frightens me." These paradoxical effects usually clear as the dosage is raised, and if an amphetamine preparation is added.

As a general rule, the adverse side effects appeared during the first 3 weeks. Patients rarely were bothered by them later in the course of treatment.

There were several exceptions to this general rule. The Parkinson-like syndrome could appear at any time providing the total daily dose was high enough. Drowsiness and fatigue also could be produced at any time depending on the total dose. Nasal congestion while usually occurring early also was seen, at times, late in the course of therapy if the dose was being elevated.

The drug had to be stopped in 25 patients due to the severity of the side effects. This is of importance when considering the over-all Improvement Rating.

The over-all Improvement Rating in this group was as follows:

Number of patients	*Improvement rating*
1	I
3	II
8	HI
12	IV

Discussion

The paper presents the results of chlorpromazine therapy as seen in routine private psychiatric practice and as such has definite limitations as well as values. Among its limitations is the fact that controls such as might be afforded by the double blind technique could not readily be used. A second limiting point is the fact that in all the patients the drug therapy was accompanied by psychotherapy of various types.

It should be noted in conjunction with this point that those treated with chlorpromazine were by far the sickest of our patients. Those who were not as ill were managed by psychotherapy alone, or in combination with the more commonly used drugs such as barbiturates or amphetamines. Patients having severe agitated depressions who were treated with chlorpromazine received purely supportive therapy in all but one case. In our experience, psychotherapy alone in patients having severe agitated depressions is rarely very effective and in many instances may be accompanied by a marked increase in the degree of agitation and depression. Therefore any marked improvement in this group could be attributed mainly to the chlorpromazine. With regard to the patients with schizophrenic illnesses, it should again be noted that the milder cases were managed with psychotherapy alone. Most of those that were treated with chlorpromazine would have required, under usual circumstances, hospitalization without delay. The psychoneurotic patients were usually treated with psychotherapy alone for from two to three months prior to the addition of the chlorpromazine.

With regard to the values of this paper, it shows the results of chlorpromazine therapy in the area of psychiatry where it is being used with increasing frequency, namely in private practice. As mentioned before, almost all the statistically significant reports on the efficacy of chlorpromazine therapy have come from the large state hospitals where the criteria for significant improvement are narrower and more limited than those that must be used in the case of patients living in a competitive society.

Our technique of evaluating the significant benefits of therapy stresses the patient's capacities of adaptation and performance both socially and vocationally. It stresses, too, the patient's abilities to obtain pleasure and pride from his performance. To be sure, it also includes an evaluation of the degree of amelioration of anxiety and other symptoms and signs. We have evaluated dream material as well, wherever possible, for it offers a good indication in many instances of the degree of the activity of the unconscious fear and hostility.

With regard to the efficacy of chlorpromazine as obtained by our techniques and graded according to the criteria presented before, it appears at first glance that about one patient out of four will obtain a complete remission or very marked improvement. If one is more discriminating and limits the use of the drug only to those patients who demonstrated marked overt anxiety, very good results (Improvement Ratings of I or II) may be obtained in about one in every three cases. On the other hand, if one would have in his treatment series a very large proportion of patients who displayed very little anxiety, his results would be very poor with as few as one in every 50

cases showing good results. Our results were not as glowing as those reported by others from private practice (12, 24). This may be accounted for, in part, by difference in the criteria of improvement stipulated in our system of evaluation, as compared with those presented by the other authors.

Of the factors effecting the success of chlorpromazine, the degree of overt anxiety is the most important. As mentioned before, the greater the anxiety (particularly if the motor component of anxiety is marked), the better are the results. It is important to note that symptoms such as phobias, obsessive-compulsive manifestations, hypochondriasis, delusions, hallucinations, etc., did not improve in most cases until the anxiety was first decreased. The degree of amelioration of anxiety necessary before the other symptoms were relieved appears to be an individual equation for a given patient.

The factor of diagnosis, whether the patient was considered psychotic or neurotic, was not important in determining the success or failure of the drug. The schizophrenic patients with marked anxiety had the same rate and degree of improvement as the very anxious psychoneurotic patients. This relationship between the degree of anxiety and the degree of improvement has been suggested previously (2, 5, 12, 18, 22, 24, 28). We do not agree with the impression that chlorpromazine is particularly efficacious in any given syndrome or diagnostic entity. It would appear that its efficacy is dependent primarily upon the amelioration of the anxiety which was at the basis of the syndrome. If the degree of anxiety to begin with was not marked, the symptomatic improvement is poor. Another factor of significance is the duration of the illness. The general rule holds that the more acute the illness, the better the chances of good results. Among the schizophrenic group, the acutely ill patient with marked anxiety, marked disorganization of thinking, difficulties with reality contact did best. Reintegration in these patients was often very striking.

In our experience, most patients have required a daily dosage of at least 400 mg. early in the course of therapy before marked improvement occurred, though as stated above we we had a few patients who responded to less than 200 mg. per day, but this was the exception. The dosages recommended in the literature vary greatly. One investigator has proposed that the daily dose in each patient be raised to between 2,000–4,000 mg. for 5–10 days (20, 21). These dosages were used entirely in a controlled hospital set up and are not applicable to private practice. At the other extreme, it has been proposed that a daily total dose of less than 300 mg. is sufficient in all but a few cases (1).

As a general rule, we have found that if a patient does not show definite signs of improvement by the time he is on a dosage of 600 mg. per day, it is unlikely that he will show any significant improvement even if the drug is raised to more than 1,000 mg. per day. However, if definite signs of improvement are seen on the lower dosages, they should be increased by degrees until the maximum benefits are obtained. This level should be maintained for at least two weeks and then it may be decreased if the clinical improvement has been maintained.

We found that one of every four patients who obtained Improvement Ratings of I or II on chlorpromazine therapy had complete or very marked exacerbation of the symptoms present prior to the use of the drug. As mentioned above, the exacerbation occurred usually during the first two weeks of treatment. It appears from our experience thus far that if the remissions last for more than three months, the chances for long-term improvement are good.

The relative merits of electroshock therapy and chlorpromazine therapy have been a source of debate. We have found that failure with chlorpromazine by no means rules out a good result with electroshock. Fifty-nine per cent, or more than half of these patients diagnosed as having schizophrenia or agitated depressions, in whom chlorpromazine failed, responded very satisfactorily to electroshock therapy and have maintained their improvement for more than three months. The relative merits of combined electroshock and chlorpromazine have yet to be clearly defined. At this time, however, we cannot confirm the reports (11, 14, 24), that combined therapy decreases the number of electroshock treatments necessary for good results.

Adverse side effects of chlorpromazine therapy were severe enough to require discon-

tinuation of the drug in one of every eight patients. This is indeed a very high percentage and points up one of the great limitations of this medication. It should be pointed out, however, that these complications are more annoying than dangerous. In our experience all have cleared rapidly when the drug was stopped. The three most alarming complications reported are jaundice, Parkinson-like states and agranulocytosis.

Chlorpromazine is a valuable addition to the armamentarium of psychiatric therapy in private practice. It is another tool which we can offer a patient, but we should not look to it as a cure-all as some of the papers in the literature would appear to have us believe.

Summary

1. One hundred and ninety-nine patients treated with chlorpromazine in private practice are reviewed.

2. Clearly delineated criteria for clinical evaluation are presented.

3. Chlorpromazine was very effective in one of every four patients treated. The degree of overt anxiety present and the duration of illness were important points effecting the degree of improvement.

4. Techniques and dosages are presented. Adequate dosages are stressed.

5. Electroshock therapy was effective in more than 50 per cent of psychotic patients in whom the chlorpromazine was ineffective.

6. Complications occurred in more than 50 per cent of the patients. The drug had to be discontinued in one of every eight patients treated.

7. Chlorpromazine is a valuable but limited tool in private psychiatric patients.

BIBLIOGRAPHY

1. Ayd, F. J., Jr.: Large doses of chlorpromazine in the treatment of psychiatric patients. *Dis. Nerv. System, 16:* 146, 1955.
2. Azima, H., and Ogle, W.: Effects of Largactil in mental syndromes. *Canad. M.A.J., 71:* 116, 1954.
3. Azima, H., and Richman, A.: Alterations of copper metabolism in chlorpromazine-treated cases. *Arch. Neurol. & Psychiat., 75:* 163, 1956.
4. Blood dyscrasias associated with chlorpromazine therapy. *J. A. M. A., 160:* 287, 1956.
5. Cohen, I. M.: Effects of chlorpromazine in psychiatric disorders. *Am. J. M. Sc., 229:* 355, 1955.
6. Delay, J., Deniker, P., and Harl, J. M.: Utilisation en therapeutique psychiatrique d'une phenothiazine d'action centrale elective (4560 R. P.). *Ann. Med. Psychol., 110:* 112, 1952.
7. Delay, J., and Deniker, P.: 38 cas de psychoses traitees par la cure prolongee et continue de 4560 R. P. Compl. rend. du Congres des Medicins Alinistes et Neurologistes, Luxembourg, pp. 19–23, July 21–27, 1952.
8. Delay, J., Deniker, P., and Harl, J. M.: Traitment des etats excitation et d'agitation par une methode medicamenteuse derivee de l'hibernotherapie. *Ann. Med. Psychol., 110:* 267, 1952.
9. Delay, J., Deniker, P., Harl, J. M., and Grasset, A.: Traitements d'etats confusionnels par le chlorhydrate de diethylaminopropl-N-chlorphenothiazine (4560 R. P.). *Ann. Med. Psychol., 110:* 398, 1952.
10. Doughty, R.: The Incidence of Jaundice Associated with Thorazine Therapy. Bulletin of Science Information Dept., Smith, Kline & French Laboratories, Philadelphia, August, 1955.
11. Ford, H., and Jameson, G. K.: Comment. Paper presented at A.M.A. Clinical Meeting, Miami, Fla., December, 1954.
12. Garmany, G., May, A. R., and Folkson, A.: The use and action of chlorpromazine in psychoneuroses. *Brit. M. J., 2:* 439, 1954.
13. Giacobini, E., and Lassenius, B.: Chlorpromazinebehandling. *Nord. Med., 52:* 1693, 1954.
14. Goldman, D.: Treatment of Psychotic states with chlorpromazine. *J. A. M. A., 157:* 1274, 1955.
15. Hamon, J., Paraire, J., and Velluz, J.: Remarques sur l'action du 4560 R. P. sur l'agitation maniaque. *Ann. Med. Psychol., 110:* 331, 1952.
16. Hamon, J., Paraire, J., and Velluz, J.: Etats anxieux et barbituriques potentialises. *Ann. Med. Psychol., 110:* 403, 1952.
17. Hoch, P., and Polatin, P.: Pseudoneurotic forms of schizophrenia. *Psychiat. Quart., 23:* 248, 1949.
18. Hoch, P. H.: The effect of chlorpromazine on moderate and mild mental and emotional disturbances. In *Chlorpromazine and Mental Health.* Philadelphia: Lea and Febiger, 1955, pp. 99–111.
19. Hoffman, J. L.: Discussion. In *Chlorpromazine and Mental Health.* Philadelphia: Lea and Febiger, 1955, p. 88.
20. Kinross-Wright, V.: The intensive chlorpromazine treatment of schizophrenia. Psychiatric Research #1 of the A.P.A., July, 1955.
21. Kinross-Wright, V.: Chlorpromazine treatment of mental disorders. *Am. J. Psychol., 111:* 907, 1955.
22. Lehmann, H. E., and Hanrahan, G. E.: Chlorpromazine: New inhibiting agent for psychomotor excitement and manic states. *Arch. Neurol. & Psychiat., 71:* 227, 1954.
23. Lesse, S.: Psychotherapy and the ataraxics. I. Some observations on combined psychotherapy and chlorpromazine. *Am. J. Psychother., 10:* 448, 1956.
24. Moyer, J. H., Kinross-Wright, V., and Finney, R. M.: Chlorpromazine as a therapeutic agent in clinical medicine. *Arch. Int. Med., 95:* 202, 1955.
25. Overholser, W.: Discussion. In *Chlorpromazine and Mental Health,* Philadelphia: Lea & Febiger, 1955, p. 174.
26. Polatin, P., and Hoch, P.: Diagnostic evaluation of early schizophrenia. *J. Nerv. Ment. Dis., 105:* 3, 1947.
27. Pollack, B.: Mental illness. *M. Times, 83:* 439, 1955.
28. Winkelman, N. W., Jr.: Chlorpromazine in treatment of neuropsychiatric disorders. *J. A. M. A., 155:* 18, 1954.

710 West 168th Street
New York 32, N. Y.

GROUP PSYCHOTHERAPY WITH PSYCHOTIC PATIENTS

H. C. KRAMER, M.D.*

Introduction

A number of young psychiatrists and psychiatric social workers have approached me asking how one starts and conducts group psychotherapy with psychotic patients. This article is an attempt to transmit some of the knowledge which I have acquired in several years of experience in this field.

Psychotherapy in whatever form applied to psychotic patients has to be modified because any approach to this type of patient will have to take into consideration some distinctive qualities as part of their condition. The therapist will achieve very little if he will, for instance, take on the attitude of the objective listener, the reserved "know-it-all," or even the kind solicitous teacher. He has to take into consideration the slowed down mental and emotional functions, the delayed reaction time, the withdrawing attitude, the oversensitivity, the emotional imbalance, the aggressive tendencies, and the ever present hostility against every enforcement of therapeutic influence. All of them may not be present in one patient, but one or more can always be detected in any psychotic patient. These characteristics will set limitations to any psychotherapeutic approach with psychotic patients as distinct from psychotherapy with neurotic patients. If the psychotherapist will not make allowances for them, psychotherapy may do the patient more harm than good.

Individual psychotherapy with psychotic patients encounters many difficulties. Transference may develop so slowly that because of the time-consuming factor, counter-transference may overwhelm the therapeutic effort and may develop into a harassing process, tiring out the patient as well as the therapist. Since the mental faculties are often severely blocked by unconscious and uncontrollable emotions, the relationship of the single patient to members of a group is of a more impersonal character, and transference and counter-transference are made easier. The emotional blocking can be well observed in group therapy sessions. It acts like a stop-cock which by turning its valve lets only a drip of the mental stream through. The emotional block reacts well to group therapy because the mental faculties have remained nearly intact in many cases and start to react when the restricting valve has been removed.

A long-standing schizophrenic patient who after prefrontal lobotomy had taken an active part in group therapy sessions gave the following written account: "I was never able to relate in public about my experiences before or after my operation. I never got close to anyone or could open up to a group of people. Now it seems so easy for me to speak up in group sessions. Maybe this is because I know all the patients so well and have listened to them for a long time. Now I do not feel embarrassed in the slightest to talk about my problems". Problems and especially common problems are some of the denominators which make group therapy an appropriate instrument in the treatment of psychotic patients. Because of their mental and emotional blocking it is very difficult for them to relate directly to others. Most of them are aware of these shortcomings, but because it touches the mental sphere, it adds more to their degradation than any other pathological symptom. The success of the publicity concerning mental diseases in our time depends upon the comforting thought that anybody else may suffer the same fate. Patients as well as their relatives draw consolation from the fact that a mental condition is a disease and not something which sets the patient apart from others.

Group psychotherapy seems especially suited in the treatment of psychotic patients because it involves an educational as well as an emotional and social stabilizing factor. Group psychotherapy does not demand from the patient complete control of his mental concentration. He may attend the sessions without being forced to direct his complete attention to the point in question. Patients participating in the sessions may become more

* Dr. Kramer died on Oct. 4, 1956

amenable to organopathic treatment, though its curative value is still debatable, because they will learn to understand it and, by interaction with a group of people subjected to similar sufferings, may improve in their human relationship and a more mature approach to life.

The Settings of Group Sessions

The setting of the group sessions is probably as individually different as are the personalities of its leaders. Yet, the setting is to a certain extent indicative of its success or failure. There is no reason to believe that a rigid formula should be applied and that any difference in the setting will have a less beneficial influence upon the outcome than any other setting. There are a few factors which, according to my experience, facilitate greatly the interrelationship of the members of the group and alleviate their hostility and aggression. A relaxing atmosphere is the first factor I would recommend. Sitting in a circle where every member faces all the other ones has become the setting of my choice. The therapist and the attending members of the nursing staff join the circle in an unobtrusive way, thus becoming an integral part of the group sessions. Their places should never be reserved or set apart from the group; they may take them as they come and may change them from session to session as the other members do. We have even discarded the ominous table because it reminds one too much of the student-teacher relationship.

For the therapist this type of setting render an excellent opportunity to observe the patients acting and reacting in a group, their relationship to other patients and the attending employees. There may be some patients who insist on sitting near the therapist or the nurse or attendant. Others will shy away from the person in authority to the farthest seat in the circle. It is obvious that the former display a great need for dependency, are craving for attention and acceptance, while the latter are probably unable to be confronted with any social gathering as yet and still tend to retire within themselves.

Clinical and social pathology are overlapping each other in the field of psychiatry. The aggressive as well as the withdrawing attitude is a clinical symptom of an immature ego formation and at the same time a sign of poor social adjustment. The feeling of belonging, in our case to a group of people who by knowledge or experience may understand the patient's motivation, their vulnerability, their tendency to fixation and frustration, should never be intercepted by an inflexible attitude.

The relaxing atmosphere, on the other hand, should not be overemphasized. I have attended group sessions which were held on a porch, or a big-sized conference room, or a big classroom. The members of the group were either standing around the therapist in informal groups, or they were sitting around an enormous conference table. In another group session, they were sitting in school benches while the therapist occupied the teachers platform. Only a small part, mainly the ones nearer the therapist, actually took part in the discussions or were attentive to them. The others, wrapped in themselves, seemed still to be engaged in day dreaming.

These types of settings are unsuitable for psychotic patients, lead easily to restlessness, inattention and self-absorption. Thus the intimacy of a small room is certainly preferable to the coldness and indifference of a vast conference room or an open porch where attention may be distracted more easily.

Technique of Group Psychotherapy

A variety of techniques of group psychotherapy sessions has been developed. This will not necessarily interfere with their results. The validity of none of them has been proved or disproved because the technique of a particular type of group psychotherapy will develop with experience, depending upon the kind of members participating in it, their ages background, sex and other conditions.

Years ago I had to conduct group psychotherapy in Edinburgh, Scotland, with two different groups of patients. The one group consisted of patients to be prepared for major surgery; the other, of problem children and their mothers. It seems evident that the approach had to be quite different. In the first group the goal to which psychotherapy had to be directed was prophylaxis of an emotional trauma which always may result from crippling operations. For the other group the aim consisted in finding the emotional trauma

which had caused the maladjustment of the child as well as his and his mother's reeducation.

The technique of any psychotherapy will also depend upon the therapist, his age, background of psychology as well as his approach and attitude. It sometimes happens that a patient will be completely intransigent toward one therapist while he may respond favorably to another. I remember the case of a twelve-year-old boy who seemed to be antagonistic toward the female therapist leading this particular group. After being changed to another group which was led by a young and vigorous male therapist, he reacted well to treatment. The exaggerated virility of a twelve-year-old boy prevented him from reconciling himself with a female leadership.

The matter of identification may also play an important role. Identification with a mother figure or a father figure will be served best with a patient who had no opportunity to identify himself with either parent. Psychotic patients who have to remain in a hospital for a long time frequently start to identify themselves with their nurses or attendants. They mirror the attendants attitude so completely that they at times rule the wards by sheer personification. This identification with an ideal figure does not always have a poorly motivated cause as a result. The case of a patient comes to my mind who returned to the hospital numerous times. On her last admission she took part in group psychotherapy sessions. The participating employee was a young intelligent attendant who had lost her husband after a long-standing illness. She had stood by him and her only child in a very courageous manner, giving him not only generously of her time and love but also her understanding. Discussing this type of human relationship, the patient seemed to have been greatly impressed by the attendant's way of life. She frequently expressed her admiration for her and begged to be transferred to the ward where this particular attendant was in charge. It seems that the patient identified herself so completely with the attendant that when she was released again from the hospital, she took up a position as a nurses aid and has not returned since. This was several years ago.

One of the best indications of a properly functioning group is the interest the patients take in the sessions. Their participation or their aversion toward the sessions are reliable tokens of their interest. This depends also to a certain extent upon the selection of the group members. Yet, experience has taught me that a too homogenous group of patients may display little incentive. Gratifying interaction of the group members does not depend upon a smooth frictionless mental discourse as the following case has taught me.

One of the patients who never had shown much interest in the discussions suddenly became disturbed. She jumped up from her chair, gesticulating wildly, accusing the others in a loud screaming voice of having trapped her. At first I was undecided as to what to do, fearing this outburst would bring about a general upheaval. However, the other patients remained completely calm, and just as suddenly as she had jumped up, the patient sat down murmuring in an embarrassed way: "I am sorry, sorry." This incident gave way to a lively discussion which culminated in the manifestation that everybody apparently has a trigger point which if touched consciously or unconsciously may lead to an emotional upset. It was exactly the case with our patient, whose paranoid trends were affected by our general discussion of persecutory ideas.

This incident points to another problem encountered frequently in group psychotherapy. Not all of the participating members take an active part in the discourse. Some may for a long time remain inactive and even at times apparently inattentive. That does not necessarily mean they have to be excluded from the sessions. Some may benefit only by listening to the discussions, and I have known quite a few who in spite of their lack of participation have been completely aware of the problems discussed.

In forming a new group, an initial interview with the patient selected may be advisable. Even if the therapist knows the patient, this preliminary interview may give him an idea if and what the patient may gain by this type of therapy. I have acquired the custom of inviting the patients instead of ordering them to participate. It makes for a better interrelationship, relinquishes the fear of any unknown treatment, and also implies being

selected for a privileged group. A patient's own desire to participate in group psychotherapy seems always a constructive incentive which should be utilized even if the prospects are not entirely favorable.

Newcomers to the group are introduced either by the therapist or another patient who was instrumental in inviting him. Even in forming a new group, a nucleus of former participants is retained. These so-called old timers are helpful in starting and carrying on the discussion until the newcomers have warmed up. They too, may explain the meaning and design of group psychotherapy to the new members at the beginning of first sessions. This kind of technique may not only change the tense atmosphere but also gives the members an idea of what to expect. We have to realize that anxiety, tenseness and a poor emotional and social relationship are the concomitants of any psychotic condition. Psychotherapy should be directed to relieve them, to aim towards a better integration of the personality and toward emotional and mental maturity.

Mode of Discussion

The way the discussions are carried out may be of importance though there need not be a rigid schedule or fixed plan set before each session. A certain scheme which helps to keep the discourse going and keep the conversants in line, however, may be of help. The patients should not only obtain a certain amount of knowledge about their condition and the eventual prevention of further attacks but should gain in insight and be able to correct their faulty judgment. They also should derive some gratification from this type of treatment. They should again acquire the feeling of being part of human society and not people set apart because of their illness. One must also try to avoid further traumatization of the patients.

In group psychotherapy the therapist does not remain inactive as is mostly the case in individual psychoanalytical treatment. He should guide the discussion, stimulate it by short and precise remarks, and should not let it slip into a mass of howl or fragmentary and scattered utterances. This may be a somewhat difficult proposition especially at the beginning of a new course. The patients not yet used to this type of verbal and free intercourse are mostly non-committal, their interrelationship is practically non-existent, the atmosphere is tense with expectation of the unknown and frequently is openly hostile. Here the skill of the therapist should come into being.

Certain factors, if taken into consideration by the therapist, should be helpful. He may conduct the sessions by establishing from the very beginning a relationship similar to a group of people sharing in a subject of interest and concern to all. He should try to exclude any rivalry by giving every member time to express his ideas and thoughts about a particular problem. He should make the group members realize that they have to listen to others if they want the others to listen to them. He should be able to join and direct the differing concepts and beliefs, and it is his supreme task to harmonize them, smooth out misunderstandings and misinterpretations. Guiding more than teaching, leading more than urging, sharing more than ruling may best describe the therapist's role in group psychotherapy.

In order that the members of a group may learn from each other, they have to accept them as equals. There will be in every group a number of patients who are able to express their thoughts in a more fluent and pertinent way. Others will be unable to do so or are inherently at a loss to express themselves precisely. Yet, the good talkers are not always the good thinkers, and every therapist will find out sooner or later that he has to strengthen and stimulate the inactive members and acquiesce the too active ones. This should be done in a gentle and calm way in order to encourage the former and discourage the later ones. An inconsistent and rejecting therapist will not only exercise spiritless influence upon the whole group but also may inflict secondary traumatization to the one or other of the members.

Topics of Discussions

The best incentive for group discussions, to start with, is questions arising from the members of the group. The patients will have to be encouraged to do so. The therapist may verbalize his own opinion and feelings about a certain problem which has meaning to every-

one. On the other hand, the discussion may sometimes center around one particular patient who has been acting out in a peculiar manner or has boasted about himself.

Take the case of a patient whose paranoid ideation was brought out by the fact that she insisted that she alone was of sound mind while all the other patients were "crazy". A discussion ensued where much repressed material was brought to the surface. She had fallen in love with a man who for a short time offered her a way of life of which she had always dreamed. He turned out to be a racketeer, married, and unable to fulfill the promises he had made to her. Deeply hurt and frustrated "she fell back on her pride". She insisted that the man had persecuted her and her family, she never gave in to him, she felt there was nothing wrong in her going to the police and FBI in order to get rid of him and his gang, he was not her equal, nobody is her or her family's equal, and so on.

One is surprised by some patients' understanding of other's problems while their own insight may still be lacking. The members of the group did become aware of the patient's extraordinary sensitivity, her projecting of her own errors upon the man, her paranoid tendencies and grandiose ideation. They felt that there was quite an unsolved hostility in her which she had to comprehend in order that her way of thinking might become more sound.

With some skillful handling, psychotic patients can be made into good conversationalists. The method of returning the question to the group for discussion is advisable and helps to inspire a general discussion of a particular problem. For instance, the first question which usually arises is: "Why have we been confined to the hospital? Why couldn't we be treated at home?" The therapist by returning the question to the group may ask: "Why do you think you have been taken to a hospital and why couldn't you have been treated at home?" This simple technique invariably produces some results and, as meager as they may be, gives the therapist some cues as to how to expand the question further.

This indirect technique leaves room for a variety of interpretations coming from the members of the group and deprives it of a one-sided critical appraisal. It eases their interaction and smooths out much of the aggression and hostility. This does not mean that the therapist should not intervene in the discussions and eventually give his own interpretation of a certain problem. After discussing a topic for quite some time, the patients may turn to the therapist and ask his opinion. This may even stimulate a new discussion from a different point of view. Thus the patients may realize that a problem has not only one aspect of interpretation, but that by discussing and considering them, one can learn more than by simple conformity. It is often enjoyable to see a patient whose negativism was an annoying factor become less objectionable and more amenable to the discussions.

I have one patient in mind who at first refused to take part in group psychotherapy as she rejected all forms of treatment. She dominated the other patients and the ward personnel, ridiculed the ones who submitted to treatment or did some work. Her haughty and arrogant manner was displayed against everybody including the psychiatrist. She was a patient with a sharp mind and a keen sense of incongruity. With such a patient it is advisable to give at first individual attention before inviting her to participate in group sessions. By individually approaching her the emphasis was placed upon her ability to grasp problems quickly and to express them fluently. Later on her deep-seated inferiority feelings were discussed which she carried around as a chip on her shoulders, compensating for them in a wrong manner. Our two way conversation resulted in her taking treatment and asking to be invited to the group sessions. She has since become a valuable member of the sessions adding inspiration by her intellectual grasp and her sense of humor which apparently developed of her sarcasm and her overbearing attitude.

It seems important that no question which arises from the group should remain unanswered. If a question does not fit into the topic of one session, it should be postponed for another one. This gives the group a pool of topics upon which the therapist can fall back if no other subject has been brought up. Yet, no question should remain undiscussed. No matter how queer and how absurd it may seem, it should not fall under the table. It is the task of the therapist to make the question intelligible.

Minutes kept of the sessions are valuable

sources of information of the subjects discussed, the discussion itself, and the interpretation of the problems involved. The minutes are kept by one patient who sketches them and works them out after the sessions with other patients helping in a joint effort. We like to read the minutes of former sessions at the beginning of a meeting especially when a problem remained unsolved or did not seem to end with a good interpretation. For the therapist these minutes are of inestimable value because they may give him a better picture of the symptomatic improvement, the individual adaptive pattern, the social adjustment, and the psychopathology of the individual case.

The topics of the sessions range from the more simple subjects concerned mainly with the personal welfare of the patients, their treatment, visitor privilege to clinical and social symptomatology. Discipline and ward routine come in for frequent criticism. As the meetings progress psychopathology and psychodynamics enter the field of conversation. At times the defenses of one or another patient break down, and they may reveal unconscious material which then becomes the basis of a general discourse. The therapist should not attempt to sidestep any topic because there does not exist a subject which should be avoided if the therapist tries to keep the discussion on a sensible and comprehensible level. If a patient wants to bring up personal problems, she should not be discouraged though no patient should ever be forced to do so. At times personal problems have a better therapeutic impact upon the other patients than general ones.

A patient with very deep-seated paranoid trends toward her mother-in-law burst forward one day with her accusations and charges. This gave way to a heated discussion about the mother-in-law problem in general. As the patient continued with her story, it soon became clear to the others that there was some peculiar motivation involved in her accusations. They found that this patient's feelings were greatly charged with jealousy, that she did not want to share anything, least of all her husband with his own mother. Her tendency to rivalry probably developed in the formative years. She seemed unable to bear the thought of being one among many, and her competitive drive always set limits in her relationship with other people.

More than with setting, technique and mode of discussions, the smooth and fluent discourse of the sessions depends upon the skillfulness of the leading therapist. Skill may increase with experience, yet the therapist of a group psychotherapy class has to be aware that not only the patients but he too is learning by mutual understanding of the problems involved.

Length of Treatment

The length of treatment of the individual patient cannot be predicted. Patients with spontaneous remissions usually react well from the beginning of treatment. They have a certain curiosity about their condition which seems so unexpected and strange to them. They are coming to the group therapy sessions openminded. First admissions with the exception of the so-called malignant cases react favorably as they usually do with any type of treatment. Paranoid patients, on the other hand, react slowly if they react at all. Their resentfulness, their feeling of omnipotence, their suspicion and oversensitivity makes them poor risks for any type of psychotherapeutic influence. That does not mean that they should not be tried, but the interplay between the paranoid patient and the other members of the group demands skill and a great deal of thoughtfulness on the part of the therapist. In between these extremes are the many shades of psychotic manifestations which may be helped to improvement and even to remission of their condition after somatotherapy has established contact with them.

The average time for which a patient hospitalized should take part in group psychotherapy is about three months, with weekly or bi-weekly sessions. If the patient has reacted favorably, continuation of group psychotherapy outside the hospital would be advisable. This may assist him in overcoming his social handicap and may give him the opportunity to belong to a group of people with similar expeience.

Some patients may acquire in a short time a rather smattering knowledge of psychotherapeutic terms and technique. Their behavior in the group betrays this apparent state of improvement, yet the unconscious conflict is still present, his judgment still faulty, and his

comprehension purely on the surface. Superficial knowledge and an agile application of it always are deceiving factors of which the therapist should be ever so much aware.

Improvement may occur by steps, and as every treatment has its aim, group psychotherapy should be directed toward the patient's ability to adjust to outside living conditions by a reconstruction of his adaptation pattern. Maturity, at least to a certain degree, should be achieved, his insight and judgment should be reestablished in order that his inner forces may be strengthened.

Not all patients can be reached even by prolonged group psychotherapy. The conflict from which they are suffering is too deep seated; their relationship to others may be completely destroyed or their superego was never built up. These patients need more than the cursory approach which group psychotherapy can offer them.

Some patients will have to be excluded from group psychotherapy after a time of observation. They may react better to individual psychotherapy, or work therapy or organotherapy will have to be reinstituted.

As with every treatment, group psychotherapy, its duration and results should not be approached dogmatically. The hospitalized patient should return to normal living conditions as soon as possible. This, too, restricts the duration of group psychotherapy in the state hospital. The patient's stay in the hospital, however, will be facilitated by the educational and social influence which group psychotherapy can exert upon him.

Criterion of Success or Failure of Group Psychotherapy

The success or failure of group psychotherapy depends as much upon external as inner factors. Is the patient able to leave the protective environment of the hospital and adjust again to a life situation which has thrown him out of emotional balance? Has he gained enough inner strength to face the stress and strain of the every-changing life outside the hospital? Nobody can predict precisely the patient's future course, and any final conclusions drawn from the study of patient's history, symptomatology, change of behavior, insight and judgment are guess work with a few exceptions.

We may expect clinical improvement in a patient whose ego has been developed yet not grown to full maturity. After organopathic treatment the ego at times emerges unscathed yet not fully matured. In other cases the ego might have been buried under the primary symptoms, repressed or projected into secondary symptoms. Traces of a superego as we may find it in patients with professional skill might also be a hopeful sign. As mentioned before, any patient who volunteers his participation in group psychotherapy and thus expresses interest in this type of therapy can be called a fair risk.

Social improvement can be expected in all cases where the with-drawing attitude, anxiety, tension and agitation are symptoms of the psychosis. Here a pleasant and relaxed interrelationship between the members of the group can be an excellent incentive for interaction with the less active members.

A young female patient with good educational background turned from "an extrovert into an introvert" while suffering from a catatonic spisode. Her prepsychotic personality was described as social, friendly gentle and convivial. The fact that she had pushed herself too much lately was probably an initial symptom of her condition. During her illness she became seclusive, shunned her family and friends, became sullen and gloomy. She responded favorably to chlorpromazine treatment clinically, but remained somewhat morose and withdrawn socially. She reluctantly took part in group psychotherapy, yet it seemed to help her regain her prepsychotic social demeanor. She was liked by everybody because of her outgoing and jovial manners.

In this case social improvement could have been expected because of her prepsychotic personality, her former social interest, and her well-developed ego which probably was buried but unscathed under her psychosis.

Paranoid patients, as difficult to treat as they are, may be helped by the indirect approach of group psychotherapy. They are excessively oversensitive and constantly on the defensive. Individual psychotherapy may end in an unbearable counter-transference situation. These patients mostly reject treatment, and if forced, it deepens their hostile attitude. Any break through this vicious cycle is in itself an achievement. The therapist has to be especially skilled

to avoid inflicting any additional trauma to their already distorted ego. A paranoid patient, whose symptoms could be traced back to her teen-age years, managed to live outside, get married and give birth to three children before she had to be hospitalized. She developed the most bizaare paranoid trends against husband, mother-in-law, and sister. On the ward she was annoying, highly repugnant and difficult to manage. She was hostile and objected to every kind of treatment. After a few individual interviews, she accepted chlorpromazine treatment and also participated in group psychotherapy. Her initial disinterest and hostile attitude gave way to great interest in the problems discussed; she was eager to pick up her married life where she had left off and has since been released. There is no doubt that her intelligence and her ego probably were brought to some maturity through interaction with the group.

Psychopathic personalities, whatever this term may mean, are difficult to treat in group psychotherapy. They try to seize every opportunity to interrupt the discussion, to draw attention to their own person, and most of all they do not learn by experience or the interaction of the group. Only a very few psychopaths may gain by close contact with the group. They may gain in self-confidence and in adequacy in dealing with others who have suffered similar feelings of inferiority and frustration. Yet, in spite of these limitations of the psychopathic patients, it is worthwhile to try group psychotherapy in selected cases.

The case of a young Negro woman comes to my mind who has been released from the hospital and has managed to stay outside. Hers was a history of violence toward everybody in authority. She had fallen in love with a married man, pursued him, and threatened him and his wife. Her distrust, suspicion and hostility did not seem to have any limits. She felt constantly frustrated, insisting that "nobody cared for her." She was very eager to participate in group therapy assuming that this was a kind of privileged treatment. In the beginning she felt uncomfortable, was tense and afraid to talk. The relaxed atmosphere and the good spirit which prevailed during sessions appealed to her favorably, and she became an active member of the group. She became attached to some members of the group and still writes to them from time to time.

The basic principles of group psychotherapy apparently lie in the modification of the transference and counter-transference situation, as a collective rather than an individual approach. The patient is no more an isolated entity facing the therapist who is a superior individual in knowledge, comprehension and emotional control. The appraisal of group psychotherapy rests with the fact that the patient learns to realize that he is not a unique and unparalleled case but one among many who suffer from the same torture and the same peculiar condition. There seems to be a comforting feeling in suffering shared by others, probably based upon the feeling of not being left alone. This is especially important in the case of psychotics who by losing the human link (emotions, ideation, social approach) with others find themselves in a strange and unusual world.

The working of these common experiences gives the problems discussed their extraordinary flavor. And even if success may not seem equal to other forms of therapy, the encouragement the patient may derive from group discussions with other patients is in itself an achievement. Though the therapist should take part in the discussions, he never should become its center. His greater knowledge should never be emphasized, and as previously stated, he should be guiding more than teaching, leading more than urging, and most of all sharing more than ruling. He should be well versed in the disciplines of medicine, psychiatry and social sciences, and last but not least good common sense which will help him to bridge the many hurdles he will encounter in group psychotherapy. The reward is his own constant gain and the patients' rehumanization which are no small satisfaction and success.

PILGRIM STATE HOSPITAL
WEST BRENTWOOD, L.I., NEW YORK

CHLORPROMAZINE THERAPY FOLLOWING TRANSORBITAL LOBOTOMY

W. H. PATE, M.D.[1]

In the past few years a large volume of literature has accumulated—both in the United States and abroad—on the applications of chlorpromazine to neuropsychiatric conditions. The results of these reported studies have demonstrated that the drug possesses definite merit in many psychotic conditions. Lehmann and Hanrahan (6) described the effect of chlorpromazine in the manic depressive, Moyer in both acute and chronic schizophrenia as well as alcoholism with extreme agitation and delirium (8, 9), Bonafede in epilepsy (1), Winkelman in senile agitation (12). This list could be extended considerably.

While most of these investigators have noted, not unexpectedly, that fewer optimal responses occurred in patients with long-standing psychoses, the correlation between chronicity and results remained unclear.

It seemed to us that a particular segment of the large patient population of DeWitt State Hospital, if treated with chlorpromazine, could help clarify this relationship. Specifically, we were thinking of those neuropsychiatric patients who, although given the benefit of transorbital lobotomy and other therapies, had not responded favorably. Unquestionably, they represented patients with the poorest prognosis since their condition had become chronic long before surgical intervention took place, and the lobotomies had been performed in nearly all cases with the hope of making them more amenable to ward routine and nothing more. Our determination to carry out this study was strengthened by the fact that none of the published reports that have come to our attention dealt, in any systematic way, with the effects of chlorpromazine in unimproved lobotomized patients. Our study began January 6, 1955.

[1] DeWitt State Hospital, Auburn, California. John C. Palmer, M.D., formerly Clinical Director, participated in the early part of this study.

Selection of Patients

Patients participating in this study were chosen in the following manner: The Charge Psychiatric Technicians of the security ward and of the wards for the moderately disturbed were asked to select their most troublesome patients. All of these patients were chronically ill, some of them for almost 30 years. The average number of years spent in a mental hospital by those who were to participate in the study was 12.8 (table 1) and of those who were to receive chlorpromazine, 11.6 years (table 2). The diagnoses of these patients ran the gamut of chronic psychoses and included the several forms of schizophrenia, involutional, senile, and post-traumatic psychoses, manic-depressive reactions, mixed psychoses, and others (table 2). All patients were problems in management, all required sedation at frequent intervals, and ECT, restraint and seclusion not infrequently. The great majority were "custodial care" type of patients, with few or no hospital privileges (table 1).

One hundred such patients were divided into 5 groups of 20; groups I, III, and V were treated with chlorpromazine; II and IV served as controls. The characteristics and pre-treatment status of the groups are summarized in tables 1 and 2. A brief description of each follows:

Group I: Patients who had responded unsatisfactorily to transorbital lobotomy performed 1 month to 6 years previously. (Given chlorpromazine.)

Group II: (Control for group I) Patients who had not responded satisfactorily to transorbital lobotomy performed from 6 months to 4 years previously. (Not given chlorpromazine.)

Group III: Patients in whom lobotomy was indicated but for whom consent to operation had not been obtained. (Given chlorpromazine.)

Group IV: (Control for group III) Patients

TABLE 1.—VITAL STATISTICS, WORK, AND PRIVILEGE STATUS IN FIVE GROUPS OF 20 PATIENTS BEFORE CHLORPROMAZINE THERAPY

Designation	Age		Years in Hospital		Status* Prior to Chlorpromazine	
	Average	Range	Average	Range	Work	Privileges
Group I	44.3	31–63	12.0	1–27	1—Ward 19—None	1—G 19—None
Group II	40.3	19–55	10.4	1–25	4—Interm. 16—None	3—G. 1—Interm. 16—None
Group III	49.5	34–69	11.8	1–29	20—None	20—None
Group IV	48.7	29–69	14.4	2–28	1—Hosp.Ind. 6—Ward 13—None	2—E 1—G 17—None
Group V	49.5	30–65	15.2	1–30	2—Hosp.Ind. 2—Ward 1—Interm. 15—None	2—E 2—G 16—None

* G—Allowed to go about hospital grounds unattended; E—Allowed to run intramural errands unattended Interm.—Intermittent privileges, revoked during disturbed periods; Hosp. Ind.—Employment in hospital industries such as the laundry, cafeterias, canteen, garden; Ward—Regularly assisting with ward work such as making beds, washing dishes on the ward, mopping floors.

similar to those in group III. (Not given chlorpromazine.)

Group V: Recently lobotomized patients started on chlorpromazine 5 to 7 days postoperatively.

METHOD

The pre-treatment records for each patient participating in this study contained the following information:

1) Ward of residence on any given date. (This served as one of the indicators of the patient's past behavior.)
2) Frequency and duration of restraint or seclusion required.
3) Frequency and number of electroconvulsive treatments required.
4) Frequency and duration of hydrotherapy (packs or continuous tub baths).
5) Kind, amount, and frequency of sedatives required.
6) Degree of participation in the various rehabilitation therapies.
7) Reliability, as reflected in his ability to use privileges appropriately.
8) Ability to participate effectively in purposeful and useful endeavor.

TABLE 2.—DIAGNOSTIC CLASSIFICATIONS, NUMBER, AND AVERAGE LENGTH OF HOSPITAL CONFINEMENT OF 60 PATIENTS (GROUPS I, III, AND V) TREATED WITH CHLORPROMAZINE

Diagnosis	Number of Patients	Average Number of Years in Hospital
Schizophrenia	8	24.0
Paranoid schizophrenia	21	8.5
Catatonic schizophrenia	8	11.0
Hebephrenic schizophrenia	3	7.0
Mixed schizophrenia	5	10.4
Simple schizophrenia	2	16.5
Involutional psychosis	2	7.5
Manic depressive	4	13.5
Mixed psychosis	1	2.0
Post-traumatic psychosis	1	17.0
Senile psychosis	1	2.0
General paralysis of insane	2	10.5
No diagnosis	2	11.0
	60	11.6

9) Degree of success or failure in extramural socialization.

By comparing these factors as recorded before and after treatment we could, in a measure, make each patient his own control. Patient groups II and IV, respectively, furnished a control factor for the "old" lobotomies (group

I) and for the lobotomy "candidates" (group III). The nature of group V (chlorpromazine administered 5 to 7 days after lobotomy) precluded any control factor other than the patient's own record.

All other modes of treatment were discontinued when patients in groups I, III, and V were started on chlorpromazine therapy. The therapeutic routines of the control groups (II and IV) remained unchanged.

There were no obvious shifts or changes in the ward personnel during the study period except for the first 11 days during which we secured the assistance of a graduate nurse and 3 psychiatric technicians. They helped for approximately 2 hours a day in administering intramuscular injections of chlorpromazine. This caused no greater disturbance in the ward routine than that occasioned by the electroshock therapy regularly administered three times a week.

Conditions beyond our control prevented a greater employment of rehabilitation therapies. For the same reason, individual psychotherapy was impossible, and we were unable even to increase the group therapy meetings. We mention these administrative details to emphasize that any reasonably prompt change in behavior must be ascribed to the effect of chlorpromazine alone and not to altered environment or other psychotherapeutic factors.

The patients comprising groups I and III were started simultaneously on 25 mg. intramuscular doses of chlorpromazine[2] given twice daily. The dosage was increased daily by 25 mg. until the sixth day, when the increase was 50 mg., giving a total dose of 200 mg. At this point the intramuscular doses were reduced at the same rate they had been increased, and oral doses were given to complement the reduced intramuscular doses. Thus, on the twelfth day the patients were receiving oral chlorpromazine only. (Subsequently, the oral dose was adjusted according to patient response.)

In the early part of our program we did not exceed a total oral dose of 400 mg. per day. As our experience and confidence in the safety of the drug grew, we increased or decreased the dosage according to individual response to the drug. Ultimately our daily dose ranged from 50 mg. to 900 mg. Most patients responded satisfactorily to doses of 300–600 mg. daily.

Group V patients were started on treatment approximately 3–7 days after transorbital lobotomy, depending on the rate of recovery and stabilization of blood pressure. In 86 per cent of the lobotomized patients a considerable drop in blood pressure occurred immediately following the operation. The dosage regimen in this group was the same as that of groups I and III. As patients became calm, doses were gradually reduced to maintenance level. Maintenance doses ranged from 50 mg. to 500 mg. per day orally. In cases where these doses proved too low and signs of incipient relapse appeared, 100 mg. of chlorpromazine was given intramuscularly once or twice a day for 2 or 3 days until the patient was once again under control. If patients were treated during an early stage of relapse, they promptly responded to increased oral doses alone; in cases where patients were lethargic or drowsy under maintenance levels and could not sustain improvement on lower doses, the concurrent administration of d-amphetamine permitted the patient to tolerate effective maintenance doses of chlorpromazine without drowsiness.

To assess the usefulness of the drug under test, we judged results on the basis of the patient's past record (items of which have been enumerated above) and the following simple criteria:

a) Was the patient well enough to be discharged?
b) Did he contribute to the hospital society and, if so, how effectively?
c) Did he merit privileges because of improved behavior?
d) Did he require as much convulsive therapy, hydrotherapy, and other therapies as prior to chlorpromazine treatment?

In addition, the patients were rated with a modified Sands-Malamud scale (7, 11) by psychiatric technicians. The items rated were: appearance, motor activity, aggressiveness, and socialization. This scale was selected because it provides the clinician with a method by which he can estimate quantitatively the effects of a given therapeutic course on a pathological process.

[2] Supplied as Thorazine by Smith, Kline, and French Laboratories, Philadelphia, Pennsylvania.

Results

Results are summarized in table 3. Of the 60 patients in the three groups treated with chlorpromazine, all but 6 showed some degree of improvement at the end of the 6-month control period. In contrast, only 1 of the 40 patients in the two control groups showed any improvement and that was of moderate degree. This table also indicates the need for long-term treatment in many cases.

A closer examination of the results reveals that in the chlorpromazine-treated groups: a)

TABLE 3.—Clinical Ratings of Patients before and after Treatment with Chlorpromazine* (Groups I, III, V) and of 40 Control Patients (Groups II, IV)

	Ratings*	6	5	4	3	2	1	0	Net Total
Group I: Lobotomy followed by Thorazine.	Before treatment	0	0	0	0	1	0	19	20
	After 1 to 6 mo. treatment	2	1	0	8	3	1	5	20
	After 6 to 12 mo. treatment	4	2	2	8	3	0	1	20
	After 12 to 14 mo. treatment	5	3	0	8	3	0	1	20
Group II: Control for I. Lobotomy —no Thorazine.	Before treatment	0	0	0	1	2	2	15	20
	At end of 6 mo. control period	0	0	0	2	1	2	15	20
	After 1 to 6 mo. of treatment	1(C)	0	1	8	2	2(D)	3	19
	After 6 to 8 mo. of treatment	1	0	1	8(E)	2	5(E)	3	18
Group III: No Lobotomy. Given Thorazine.	Before treatment	0	0	0	0	0	0	20	20
	After 1 to 6 mo. treatment	1	1	1	8	3	6	0	20
	After 6 to 12 mo. treatment	3	1	0	9	2	5	0	20
	After 12 to 14 mo. treatment	4(A)	1	0	9	2	5	0	20
Group IV: Control for III. No lobotomy. No Thorazine.	Before treatment	0	0	0	0	1	6	13	20
	At end of 6 mo. control period	0	0	0	0	1	6	13	20
	After 1 to 6 mo. of treatment	0	0	0	8	6	4	2(F)	18
	After 6 to 8 mo. of treatment	1	0	1	7	6	3	2(F)	18
Group V: Lobotomy followed immediately by Thorazine.	Before treatment	0	0	0	3	2	1	14	20
	After 1 to 6 mo. treatment	2	1	0	11	2	3	1	20
	After 6 to 12 mo. treatment	6	4	0	7	1	2	0	20
	After 12 to 14 mo. treatment	8(B)	4(B)	0	8	0	3	0	20

* Legend:

6—Out of hospital and contributing to society.

5—Out of hospital but requiring some supervision.

4—Doing efficient work in hospital industry; approved for leave of absence or family care; maximum privileges.

3—Doing efficient work in hospital industries; maximum privileges.

2—Fairly efficient worker on ward or in hospital industries; limited privileges.

1—Improved conduct; no productive endeavor; no privileges.

0—Unimproved.

(A)—1 patient subsequently returned from extramural care.

(B)—3 patients of the 12 subsequently returned from extramural care.

(C)—Subsequently returned to hospital.

(D)—1 discontinued because of unrelated illness.

(E)—1 patient discontinued because of severe recurrent dermatitis.

(F)—1 patient died of cause not related to treatment and 1 patient transferred off of service due to fractured femur.

TABLE 4.—RATINGS OF FIVE GROUPS OF PATIENTS ON BASIS OF THE SANDS-MALAMUD SCALE

Group Designation	Average Score prior to Treatment	Average Score after 3 Weeks of Treatment	Average Score after 9 to 12 Weeks Treatment
Group I Old lobotomy, chlorpromazine therapy.	8.6	4.1	2.5
Group II Old lobotomy, no chloropromazine.	7.2	7.6	7.4
Group III No lobotomy, chlorpromazine therapy.	6.6	3.4	2.2
Group IV No lobotomy, no chlorpromazine.	5.9	5.4	5.4
Group V Recent lobotomy, chlorpromazine therapy.	Incomplete	3.5	2.2 (4 to 12 wk.)

13% of the patients improved to the extent that they could be discharged from the hospital; b) 47% were doing efficient work in the hospital's industries and enjoyed maximum privileges in the hospital; c) 13% were contributing in some measure to the hospital industries and had limited privileges; d) 17% improved in conduct only; e) 10% showed no improvement.

Since the introduction of chlorpromazine therapy, there has been no need in the treated groups for restraint, seclusion, EST, hydrotherapy, or sedation of any kind.

In the control groups the clinical ratings remained virtually unchanged (table 3) although, as mentioned earlier, their therapeutic routines (EST, hydrotherapy, sedation, reserpine) continued throughout the period of study.

The results of the Sands-Malamud rating are shown in table 4. The improvement in the average score of patients in group I, II, and V is striking. The differences between the 3-week and 9 to 12-week scores emphasize another factor in chlorpromazine therapy, namely, that for maximum efficacy the drug should be administered for a minimum period of 2 months and often longer (table 3). This has been pointed out previously by Goldman (4).

SIDE EFFECTS

There were very few complaints of pain or discomfort due to injections until doses of 150 mg. (6 cc.) were given over a course of several days. With such doses considerable inflammation at the site of injection occurred in some patients as well as tenderness on touch. Inflammation promptly subsided when the injections were discontinued.

Transitory orthostatic hypotension occurred in a few patients on large intramuscular doses who inadvertently managed to get out of bed a few minutes after an injection. They simply slumped to the floor. None was injured, and none manifested alarming signs. The only treatment necessary was to put them in a recumbent position.

There were a few cases of dermatitis, usually characterized by discrete red papules about 1 mm. in diameter and of similar height. The rash tended to disappear after several days, even when therapy was continued. One psychiatric technician developed localized dermatitis after handling the tablets. A patch test confirmed her sensitivity to chlorpromazine.

There were 3 cases of distressing dermatitis which resembled urticaria with patchy distribution of elevated, closely-set, irregular erythematous areas. In 2 of these the minute papules, described above, filled the erythematous areas. The areas involved were those most prominently exposed to light. The arms and legs were more seriously affected than the neck and face, while the thighs and the trunk remained relatively free. A third case presented characteristic symptoms of an allergic reaction: fever (rectal temperature 104°F.), marked swelling of the face and neck, generalized mild erythema, itching, etc. The patient responded to antihistamines within 3 days. In all three patients, resumption of chlorpromazine treatment did not bring about a recurrence of dermatitis. Aggravation of a of a pre-existing dermatitis ultimately led to abandonment of treatment in one case in

which an excellent remission of symptoms was taking place.

Several cases suggestive of Parkinsonism occurred. Doses were immediately reduced, and the moderate tremor, muscular weakness, stooping posture, and diminution of accessory movements subsided. Prominent Parkinsonism-like syndromes occurring in connection with chlorpromazine therapy have been described by Moyer (10), and Kinross-Wright (5).

Discussion

In many of the patients whom we have treated with chlorpromazine a reintegration of personality characterized by recession of delusions, hallucinations, and other overt psychotic manifestations seemed to develop. Certainly an action like this should not be labeled as merely "sedative". Fabing has suggested on several occasions (2, 3) that the action of the drug be called "ataractic", that is, one creating calmness or tranquility untroubled by mental or emotional excitation, and our experience is in agreement with such a description.

Concurrent with reintegration of personality among the treated patients the destruction of property and clothing rapidly declined, as did soiling. The change was also reflected in elimination of the need for electrotherapy and sedatives, for time-consuming and costly maintenance, and for the laundry burden. The savings which accrued from this transformation were not directly measurable because they involved such intangibles as improved morale of personnel, better receptivity of the patients to psychotherapy, a more cheerful atmosphere on the wards, and so on.

The unusual and highly successful results that were achieved by administering chlorpromazine to mental patients with records of long-standing illnesses and virtually hopeless prognoses force us to re-evaluate our disposition toward such patients. No longer should they be regarded as objects of mere custodial care, but as groups of human beings in which 5 out of 6 can be returned to a much improved social setting. Our results further showed that 1 out of 5 of the improved patients is likely to "earn his keep" in full on return to society; the other 4 will contribute in varying measures toward their upkeep—either in a home or a hospital setting. While not a "cure-all", the success of chlorpromazine therapy in "hopeless" patients was such that the arrival of this drug must be regarded as a major incident in the progressive evolution of therapeutic measures for the mentally ill.

Summary and Conclusions

One hundred chronic psychiatric patients were selected from the disturbed wards of DeWitt State Hospital and divided into five groups of 20 for a controlled study of the effects of chlorpromazine.

The five groups consisted of: 1) Patients who had responded unsatisfactorily to transorbital lobotomy performed 1 month to 6 years previously (given chlorpromazine). 2) (Control for 1) Patients who had not responded satisfactorily to transorbital lobotomy performed from 6 months to 4 years previously (not given chlorpromazine); 3) Patients in whom lobotomy was indicated but for whom consent to operation had not been obtained (given chlorpromazine); 4) (Control for 3) Patients similar to those in 3 (not given chlorpromazine); 5) Recently lobotomized patients started on chlorpromazine 5 to 7 days post-operatively.

Results showed that 54 of the 60 patients treated with chlorpromazine improved to various degrees, 9 of them sufficiently to be discharged from the hospital, considered for leaves-of-absence, or for release under family care at the end of 6 months treatment. More prolonged treatment showed a much larger number responding (table 3). Of the 40 patients in the two control groups only 1 improved.

All of the patients were also rated with a modified Sands-Malamud test, the results of which paralleled the above findings.

On the basis of these results we conclude that chlorpromazine is an effective therapeutic agent in the treatment of chronically disturbed patients who have failed to respond to psychotherapy, convulsive therapy, and transorbital lobotomy. In the last instance, it can also be thought of as having additive therapeutic value in those cases where the lobotomy was not a full success.

BIBLIOGRAPHY

1. Bonafede, V. I.: Chlorpromazine (Thorazine) treatment of disturbed epileptic patients. *Arch. Neurol. & Psychiat., 74:* 158–162, 1955.
2. Fabing, H. D.: A new blocking agent against the development of experimental LSD-25 psychosis. Read at the A.P.A. Regional Research Meeting, Galveston, Texas, Feb. 18–19, 1955.
3. Fabing, H. D.: Designation of "Tranquilizing agents" in neuropharmacology. *J. A. M. A., 158:* 1461, 1955.
4. Goldman, D.: Treatment of psychotic states with chlorpromazine. *J. A. M. A., 157:* 1274–1278, 1955.
5. Kinross-Wright, V.: Complications of chlorpromazone therapy. *Dis. Nerv. System, 16:* 114–119, 1955.
6. Lehmann, H. E., and Hanrahan, G. E.: Chlorpromazine: New inhibiting agent for psychomotor excitement and manic states. *Arch. Neurol. & Psychiat., 71:* 227, 1954.
7. Malamud, W., and Sands, S. L.: A revision of the psychiatric rating scale. *Am. J. Psychiat., 104:* 231–237, 1947.
8. Moyer, J. H., Kinross-Wright, V., and Finney, R. M.: Chlorpromazine as a therapeutic agent in clinical medicine. *Arch. Int. Med., 95:* 202, 1955.
9. Moyer, J. H., Kent, B., Knight, R., Morris, G., Huggins, R., and Handley, C. A.: Laboratory and clinical observations on chlorpromazine (S.K.F. 2601-A), hemodynamic and toxicological studies. *Am. J. M. Sc., 227:* 283–290, 1954.
10. Moyer, J. H.: The pharmacology of chlorpromazine. *Internat. Rec. Med. & Gen. Prac. Clin., 168:* 301–311, 1955.
11. Sands, S. L., and Malamud, W.: A rating scale analysis of the clinical effects of lobotomy. *Am. J. Psychiat., 105:* 760–766, 1949.
12. Winkelman, N. W., Jr.: Chlorpromazine in the treatment of neuropsychiatric disorders. *J. A. M. A., 155:* 18, 1954.

Box 192
AUBURN, CALIFORNIA

RESERPINE AND METHYLPHENIDYLACETATE EFFECTS ON SOCIALIZATION AND ACTIVITY

G. DONALD NISWANDER, M.D.,[1] GEORGE M. HASLERUD, PH.D.,[2] NATHAN BRODY, B.A., AND THOMAS M. CASEY, B.A.

It is generally felt that patients receiving reserpine[3] will experience a decrease of energy output and activity. Methylphenidylacetate, hereafter referred to as Ritalin, is often added to reserpine to counteract the decreased energy output while maintaining the ataractic effects of reserpine. This study has been designed to test the degree to which reserpine, in comparison with placebo medications, and combined reserpine-Ritalin will change the amount of activity and socialization of acutely ill mental patients. The rationale for the use of Ritalin in combination with reserpine suggests the following hypotheses:

1. Activity decreases when patients receive reserpine.
2. Socialization decreases when patients receive reserpine.
3. Activity increases when patients receive combined reserpine-Ritalin in comparison with reserpine alone.
4. Socialization increases when patients receive combined reserpine-Ritalin in comparison with reserpine alone.

No clinical test was made to record the degree to which Ritalin increases or attenuates the clinical effectiveness of reserpine, and this study is not designed to answer this question; however, the use of Ritalin with reserpine leads to the following hypothesis:

5. Ritalin, added to reserpine, does not effect the ataractic quality of reserpine.

The observations for this study were made in the occupational therapy clinic of the hospital. While it approximates a real life-work situation, the occupational therapy clinic affords an opportunity for systematic, controlled, behavioral observations.

Our study and methodology were not designed to measure the clinical effectiveness of reserpine and combined reserpine-Ritalin, but to measure the several aspects of the behavioral changes induced by these medications.

This study utilizes three techniques not usually associated with clinical evaluations.

1. Each individual received placebos and, therefore, acted as his own control. This procedure eliminates the problem of individual differences in response to the medication. This group of 20 patients is the equivalent of a group many times its size in which patients are divided randomly into controls and experimentals.
2. This study employed quantified rating scales upon which reliability checks were made. The use of quantifiable rating scales afforded the chance for a statistical analysis. Standard scores for each patient on each of the medications were obtained.
3. The use of time sampling to rate patients' activity and socialization makes a mathematically valid measure of patients' output.

The rating scales and the time sampling techniques were evolved and modified from a previous study (Dixey *et al.* (1)), which evaluated changes in mental patients' behavior in the occupational therapy clinic.

The use of quantifiable experimental techniques raises the question of what role such procedures should play in the current problem of drug evaluation. As the question of general effectiveness, as indicated by clinical evaluations, becomes solved, there arise questions of a more specific type in relation to the effects of different medications. The use of experimental techniques and the conceptualizations

[1] From the Arthur P. Noyes Institute for Neuropsychiatric Research, New Hampshire State Hospital, Concord, New Hampshire.

[2] Professor of Psychology, University of New Hampshire, and Research Consultant for the Noyes Institute.

[3] Drugs for the study were supplied by Ciba Pharmaceutical Products, Inc., Summit, New Jersey, as Serpasil (reserpine) and Ritalin (methylphenidylacetate), both registered trademarks of the company.

and specialized methodology of the behavioral scientist appear to be an invaluable supplement to the clinical psychiatric evaluation.

Procedure

Subjects. Ten male and ten female patients, who were recent admissions to the hospital, were selected for the study. The age range was from 22 to 65 years, with a median age of 41 years. Length of time in the hospital for this group of 20 patients varied from 3 to 98 days, with the median hospitalization time of 13.5 days. None of these 20 patients had received treatment for their mental disorder.

The diagnoses of the group represented a cross-section of psychiatric disorders seen in an admission service of a mental hospital. Table 1 shows the various diagnostic categories of patients included in the project.

Male and female groups of patients were divided into two groups to follow two medication plans. One-half the male group and one-half the female group were on one plan, while the other groups followed the second plan. The medications were supplied as tablets labeled A, B, C and D. The placebo tablets appeared identical to the real medication. The code to the medications was known only to one of the authors (G. D. N.). Ward personnel and the observers were unaware of the meaning of the code until the termination of the project. Thus a "double blind" technique was used in relation to the medication plan. Table 2 illustrates one of the medication plans employed in this study.

TABLE 1.—Diagnosis of Patients

Schizophrenic reactions	
Chronic undifferentiated type	4
Paranoid type	3
Catatonic type	1
Psychoneurotic reactions	2
Chronic brain syndromes with psychosis	
Arteriosclerotic type	2
Alcoholic type	1
Unknown type	1
Manic depressive reaction, manic	1
Involutional psychotic reaction	1
Psychotic depressive reaction	1
Acute brain syndrome, alcohol	1
Personality pattern disturbance	1
Mental deficiency, moderate, with psychosis	1
	20

TABLE 2.—Medication Plan*

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
BD	BD	BD	BD	AC	AC	AC
AC	AC	AC	AC	BD	BD	BD
BD	BD	BD	BD	AC	AC	AC
AC	AC	AC	AC	AD	AD	AD
AD	AD	AD	AD	BD	BD	BD
BD	BD	BD	BD	AD	AD	AD
AD	AD	AD	AD	AD	AD	AD

* A, reserpine; B, reserpine placebo; C, Ritalin; D, Ritalin placebo. As shown in above table, each patient received placebos for 3 weeks, reserpine for 2 weeks, and combined reserpine-Ritalin for 2 weeks.

A fixed dosage of reserpine (4 milligrams daily) and Ritalin (20 milligrams three times daily) was chosen at the beginning of the project for all patients. The dosages for the medications were selected on the basis of one of Niswander's previous clinical experiences in treating acutely mentally ill patients. At the outset of the project, it was decided to manipulate the dosage of each medication only in the face of untoward side reactions, or when the clinical picture warranted an increase in medication, for example, continued disturbed behavior.

Only one patient required a dosage change. Due to ward management problems this patient received 7.5 to 10 milligrams of reserpine during a six-day period, and also had to be given reserpine during one of his placebo periods. As a result, this particular placebo period was excluded in the statistical analysis. No undesired side effects resulted in any patients during the project.

During the course of the study there were several periods when some of the patients could not be present for their occupational therapy clinic. Although a few of the patients were transferred to other mental hospitals as the study neared its termination point, 19 of the 20 patients were present often enough to obtain their reactions to each of the three medications. Patients were allowed all privileges in the hospital other than regularly scheduled occupational therapy clinics. No other medications were given the patients. Some of the patients attended group psychotherapy and some were allowed week-end visits home. It is obvious that there were several variables accounting for patients'

behavior which were not controlled; however, since the medications should balance each other out in seven weeks, it is reasonable to assume that influences other than the independent medication variable should balance each other out.

Three scales and one independent measure were devised for use in this study: Scale I, to measure activity; Scale II, to measure socialization; Scale III, to measure combined activity and socialization; and a fourth measure to record situations in which the patient was considered completely withdrawn.

Each item on the four different behavioral measures was assigned on arbitrary a priori value, which in the course of the study proved to be adequate. These values were designed to differentiate the relative amounts of socialization, activity, combined activity and withdrawal on the basis of two weeks of previous observations in other occupational therapy clinics.

The arbitrary numerical weightings assigned are in parentheses at the beginning of each measure of each scale evaluated during the observation periods.

The scales were as follows:

Scale I—Patient activity

a. (30) Destructive hyperactivity, e.g., breaking and throwing things.

b. (20) General overactivity. Patient is overactive to the degree that his task performance is impaired.

c. (15) Expressive constructive activity on an appropriate occupational therapy task.

d. (10) Expressive constructive activity on a non appropriate occupational therapy task. Behavior in the occupational therapy clinic in which the patient brings outside work of a type not appropriate for the most effective use of the occupational therapy clinic hour was rated in this category, e.g., a patient who would bring a book to the clinic and read would be rated in this category.

e. (5) Underactivity on an occupational therapy task. Sporadic attempts to perform task with no consistency and minimal work output.

f. (3) Sporadic underactivity performed on a non-occupational therapy task.

g. (0) Absence of activity.

Scale II—Socialization

h. (20) Verbal socialization with another patient or patients.

i. (15) Verbal socialization with therapist(s).

j. (10) Non-verbal socialization with another patient or other patients, a passive involvement with activities of others, such as working in a group but not talking.

k. (5) Non-verbal socialization with therapist(s).

l. (0) Absence of socialization.

m. (−19) Negative interaction, verbal or non-verbal aggression against patient(s) or therapist(s). Withdrawal from the social advances of others when presented.

The third scale used is an outgrowth of Scale I and II. When activity and socialization occur simultaneously, they give rise to a Gestalt-like difference in behavior compared with activity of socialization occurring separately.

Scale III—Combined socialization and activity

n. (20) Activity and verbal socialization with patients.

o. (15) Activity and verbal socialization with therapist.

p. (10) Activity and non-verbal socialization with patients.

q. (15) Activity and non-verbal socialization with therapist.

r. (0) Absence of combined activity.

s. (−9) Activity and negative interaction or refusal to respond in a social interactive situation.

t. (−19) The number of time samplings in which the patient was com-

pletely withdrawn or self-preoccupied.

The "III-t" rating was also separated out as a fourth measure because of its significance.

Each patient was rated seven times during the course of the clinic hour on each of the scales. Thus the data consist of an activity score, a socialization score, a combined score, and the number of time samplings each patient was completely withdrawn, for each of the patients for each of the 21 experimental clinic periods. These scores are not qualitative judgments of behavior; rather, they are quantitative statements about the amount of different types of behavior.

A male and female occupational therapy clinic was utilized for the corresponding group of patients. Each clinic was staffed with a female occupational therapist and a female occupational therapy student. The same therapist and student were present for all of the sessions. Two of the authors (T. M. C. and N. B.), who are psychology graduate students, acted as observers for each clinic. One observer remained in the male clinic throughout the study and one in the female clinic. The observer attempted to be as unobtrusive as possible. He was seated in a remote section of the clinic which afforded him a view of each patient's behavior. The observers attempted to remain withdrawn and did not initiate any conversation.

The patients, the occupational therapist, and the occupational therapy student were each sampled according to the following schedule: Ten seconds for observation and 20 seconds to record the observation on the four scales for each individual. The complete round of all ten patients and the two therapists required six minutes. Seven such periods occurred during the clinic hour.

Experimental clinic sessions were held Monday, Wednesday and Friday for seven weeks. These sessions were set up as follows:

1. Patients arrived as close to 8:30 as possible.
2. First observation began at 8:35.
3. At 8:47 the therapist and her assistant assumed a passive role. In this period they did not attempt to initiate any patient activity. However, they answered questions.
4. At 9:05 the therapist and her assistant assumed their normal role.
5. At 9:11 cleanup time was announced.
6. At 9:17 the observation period ended.
7. The clinic period was completed at 9:20.

This 50-minute period closely approximates the normal occupational therapy clinic period. Data relevant to the occupational therapy observation and patient behavior during active and passive periods will be published separately, to compare the effect of the professional activity of the occupational therapist on the behavior of mental patients, as previously studied by Dixey *et al.* (1).

Results

Reliability checks on the scales used were made during the early part of the experiment. Both observers seated themselves in a regularly scheduled occupational therapy clinic and independently rated the behavior of the same 10 patients. Table 3 reveals the reliability results.

In order to take advantage of the fact that each patient acted as his own control and yet make statistical examination of the effects on behavior of the different medications, all the daily scores on the various scales were changed to standard scores. The mean and the standard deviation from the whole 21 clinic days were computed for each scale for each individual. Then, for example, the average deviation of the placebo days subtracted from the general mean was divided by the standard deviation to make the placebo standard score. Similarly standard scores for the various medications were obtained. One

TABLE 3.—Reliability Results

a. Activity scale	Includes complete agreement on 164 observations out of an attempted 180, and thus accounts for a reliability coefficient of .91.
b. Socialization scale	Includes complete agreement on 160 observations out of an attempted 172, and thus accounts for a reliability coefficient of .93.
c. Combined scale and withdrawal scores	Includes complete agreement on 155 observations out of an attempted 172, and thus accounts for a reliability coefficient of .91.

TABLE 4.—SIGNIFICANCE OF DIFFERENCES BETWEEN PLACEBO AND MEDICATION WEEKS

	Male		Female	
	Reserpine	Reserpine-Ritalin	Reserpine	Reserpine-Ritalin
Activity	None	None	None	None
Socialization	None	None	Less*	None
Combined	None	None	Less*	None
Withdrawal	Less†	None	None	None

*$p < .05$.
†$p < .01$.

TABLE 5.—SIGNIFICANCE OF DIFFERENCES COMPARING RESERPINE-RITALIN TO RESERPINE MEDICATION WEEKS, WITH RESERPINE-RITALIN AS FRAME OF REFERENCE

	Male	Female
	Reserpine-Ritalin	Reserpine-Ritalin
Activity	None	None
Socialization	None	Increased*
Combined	None	Increased*
Withdrawal	Increased*	None

*$p < .05$.

can then meaningfully combine the standard scores from all subjects on one kind of medication. The results of such analyses are shown in tables 4 and 5.

Table 4 shows the significance of differences when placebo medication weeks are compared to reserpine medication weeks and combined reserpine-Ritalin medication weeks.

Table 5 shows the significance of difference when the combined reserpine-Ritalin medication weeks are compared to the reserpine medication weeks, with the former as the frame of reference.

A preliminary study of the time required for the medications to affect behavior was made by comparing the Friday clinic scores (24 hours after a change in medication, see table 2) with those for the following Monday and Wednesday. When measured by the sensitive indices of "withdrawal" in the male group and "socialization between the patients" in the female group, certain trends are suggestive even though this subdivision of the data makes the numbers too small for any test of statistical significance. The change to placebo brought noticeable effect within 24 hours, suggesting rapid elimination of the Ritalin. The addition of the active drugs after a placebo week, however, showed mounting effect from Friday through Monday to Wednesday.

DISCUSSION

The high reliability coefficients obtained indicate that the four quantified scales were sufficiently objective that the two observers could use the scales on the samating of beget approximately the same re patient and havior. The use of the "double blind" eliminated the possibility of bias.

It was hypothesized that reserpine alone would decrease activity, but our study failed to differentiate levels of activity between placebo and reserpine weeks. However, the hypothesis that socialization would be decreased when patients received Reserpine alone was supported at the .05 level (see table 4). While activity was not affected by reserpine in the female patients, the character of the individual's work in relation to spontaneity and inclination for social intercourse appeared affected. The authors feel that the reason for the difference in reaction in the two clinics was not a result of sex difference in response to the medication but rather a function of the different clinic set-ups. The female clinic tasks were mostly of a mechanical type (e.g., sewing and knitting) with which the patients were already familiar. This allowed the females more time to socialize. Most of the male patients performed tasks that were new to them (e.g., leatherwork, weaving or woodwork) or that required real concentration and attention. As a result there was less socialization in the male clinic. The female clinic, therefore, offered a more sensitive measure of the amount of spontaneous desire on the part of the patient to interact socially. The male clinic socialization scores were composed more of interaction between patients and therapists concerning instruction about task procedures. This appears to explain the difference in reaction to the medications between the male and female group.

The third hypothesis, that combined Ritalin-reserpine medication would increase activity over that for reserpine, was not sub-

stantiated (see tables 4 and 5). The increase of socialization predicted in the fourth hypothesis was obtained in a significant amount when combined reserpine-Ritalin was administered to the female group. This suggests that Ritalin combined with reserpine can be effectively used to increase socialization if it is decreased by the use of reserpine alone.

The fact that reserpine decreased the amount of complete withdrawal in the male patients is in line with the general clinical reports of the action of reserpine (see table 4). The interesting finding is the attenuation of reserpine's effectiveness by the addition of Ritalin in the male group (see table 5). In relation to the fifth hypothesis, it would appear that there is some possibility that Ritalin decreased the effectiveness of reserpine. Our study was not designed to answer this question, and our finding is an incidental by-product of our other results. However, the possibility that Ritalin may have some counteractive effect in the ataractic propensity of reserpine is strongly suggested by the increase of complete withdrawal in patients receiving combined reserpine-Ritalin as compared to reserpine alone. This finding definitely suggests the need for a comprehensive clinical study of the effectiveness of reserpine as compared to combined reserpine-Ritalin. The disparity between the male and female results in the withdrawal scores can again be explained by differences in the male and female clinics. Since the female activities were less challenging and of a more familiar nature, there were many more occasions when the females took breaks that were rated as complete withdrawal. In the male clinic where the tasks were more challenging, the number of complete withdrawals was less. Therefore, withdrawal in the male clinic appeared to be a more pathological phenomenon and would occur ordinarily in a male patient only when he was self-preoccupied. This accounts for the decrease in withdrawal when reserpine was given. On the other hand, in the female clinic where complete withdrawal appeared to be more associated with boredom, reserpine had no effect on that variable.

On the basis of our experience with the different activities on the two occupational therapy clinics, we feel it is extremely important for any future research projects, utilizing the occupational therapy clinic as a research laboratory, to make an effort to offer tasks which will provide a similar challenge in order that male and female clinic data will be more comparable.

Summary

Results are reported in a group of 20 acute patients who were observed in a series of occupational therapy sessions, and who were rated by time sampling rating scales to determine the effects of reserpine and combined reserpine-Ritalin medications in comparison to placebo medications on socialization and activity. Reserpine and combined reserpine-Ritalin have no effect on the activity output of acutely ill mental patients. Reserpine decreases socialization, and Ritalin can be used in conjunction with reserpine to offset the decreased sociability when patients receive reserpine alone. On the other hand, there is a possibility that Ritalin in some patients may have an attenuating effect on the ataractic effectiveness of reserpine. The authors believe, on the basis of their study, that rigidly controlled experimental situations with quantifiable data have a legitimate role in drug evaluation.

The authors wish to express their appreciation to the Research Council of the Arthur P. Noyes Institute for Neuropsychiatric Research, for the helpful suggestions in setting up the study and the preparation of the manuscript.

BIBLIOGRAPHY

1. Dixey, E., Haslerud, G. M., and Brown, N. C.: The effect of the professional activity of the occupational therapists on the behavior of mental patients. *Am. J. Occup. Ther.* (In press).

105 Pleasant Street
Concord, New Hampshire

THE PSYCHOSIS OF GENERAL PARESIS[1]

A Case Study and Discussion

LAWRENCE CLAMAN, M.D.

The psychosis of general paresis has long been considered by most of the medical profession as a classic form of organic psychosis. Nevertheless, during the past three decades some interest has been shown in the psychodynamics of this mental illness and a great deal in its treatment.

Many theories (1, 2, 3, 4) have been suggested over the years to explain the psychosis and have been discussed in the literature (3, 6). Early theories were based on various postulated organic factors including a specific neurotropic strain of the spirochete and differential vulnerability of nervous tissue to syphilitic invasion. Overnutrition of the cortex, central hyperemia and a treponema toxin were said to "cause" the ideas of grandeur. Later theories were placed on a combined organic and psychodynamic basis, but are incomplete, poorly integrated, and difficult to compare because of their different frames of reference.

Hollos and Ferenczi (2) were the first to attempt a psychodynamic explanation of the psychosis. They considered general paresis a pathopsychosis in which the patient responded to the impairment of his mental functions by withdrawing libido from the functions concerned. He regressed to a stage of psychic development in which the damaged functions were not yet existent and was thereby able to maintain his self-esteem. The organic damage initiated the psychosis, which then followed the psychological laws of regression, and was therefore reversible (3).

Schilder considered dementia the core of the psychosis, that damage to the brain system which accounts for thought production, anticipations, censure and reality testing allowed for the ready penetration of preconscious wishes. He felt that the case histories showed the importance of the previous personality development in the makeup of the psychosis, and that the luetic damage and psychic dissolution were equated in the patient's mind with masturbation and incestuous wishes. Schilder was evidently thinking here of the mind structurally as being composed of a conscious and unconscious without any further theoretical differentiation.

And finally, Coriat (1) thought of the psychosis as the result of an irreversible brain disease. He felt the cortical damage caused the ego to lose some of its capacity to carry out repression as well as some of its reality-testing relationship with the outside world, and that the superego was "shattered" so that "the ego was overwhelmed by the wishfulfilling forces of the id." The end result was that the patient regressed back to a narcissistic level where he lived in a world of exaggerated and distorted phantasies analogous to a dream world. He agreed with Schilder that the patient carried with him the painful consciousness of his syphilitic infection, and that he protected his ego from a sense of guilt by forgetting the infection and delusionally transferring it to an innocent source.

Because of the rarity with which paretic patients have been studied intensively from a psychodynamic point of view, it was thought of interest to present a patient with general paresis who had a schizophrenic type of psychosis and received psychological treatment for two and a half years. The demonstrable psychodynamics of this single case will be discussed, and then a revised theoretical formulation of the psychosis will be presented using earlier theories and the findings of this case.

Case Presentation

X is a 32-year-old white male, cotton mill worker and WWII veteran, who was admitted to the Neurology Service of the Boston Veterans Administration Hospital in 1954 as a transfer from another hospital. He had a two-month history of mental confusion, forgetfulness, awkwardness and clumsiness.

[1] From the Psychiatry and Neurology Service, Veterans Administration Hospital, Boston, Massachusetts.

According to his wife, for a period of eight months prior to his hospitalization he had been sporadically forgetful and mildly irritable. This had not been any cause for concern until two months prior to his hospitalization when he awoke in the middle of the night and turned "white as a sheet". He felt he was having a heart attack, but an examination by a local physician was negative. This was the first of several such attacks. With the passage of time, his confusion and forgetfulness became more pronounced so that, for example, he would ask for his shirt when he already had it on. He became irritable, deficient and awkward on his job, was often found staring off into space, fumbled objects, and was occasionally seen off balance. At home he began lying, giving inappropriate answers to questions, and was seen talking to himself. He complained of frontal headaches, developed severe insomnia, became impotent, and lost 30 pounds in a two-month period. About one month prior to his hospitalization, his wife found him locked in his room looking at sex magazines and drawing lewd pictures of women. During the week prior to his hospitalization, he smashed down a door on one occasion, and tried to strangle his wife on another. After the latter incident, he told his wife he had not known what he was doing, and this precipitated his immediate hospitalization.

He was admitted to a hospital where his confusion became more marked and he appeared to be responding to hallucinations, though some of the time he was clear. His initial examination and studies indicated the presence of intracranial pathology, and after ten days he was transferred to this hospital. At that time a spinal fluid serology was reported as positive and the colloidal gold curve as flat.

Both the husband and wife's initial premarital Wassermann tests were positive. They were treated by a local physician with one injection of penicillin weekly for six weeks prior to their marriage, and their serologies became negative. From then on the wife had periodic blood Wassermanns which were negative, but the patient consistently refused to be checked. There is no history of a primary lesion.

Past history and premorbid personality

The patient was the eldest of four boys, the youngest of whom died of pneumonia as a baby. The mother described his infancy and childhood as normal.

The father was in his fifties, an insurance agent, who left his wife and family when the patient was 15, went to California, got a divorce and remarried, but is now separated again. He was a strict disciplinarian with his children. The patient always resented his father for deserting the family because of its effect on his mother and him. She became a heavy drinker, and he had to leave school and go to work to help out financially. On the other hand, the two younger brothers always bragged about the father and were happy to see him.

The mother was in her fifties, worked as a hospital kitchen helper. Her second husband was an alcoholic, had a prison record, abused her, and there have been intermittent separations. The patient physically defended the mother on more than one occasion against the stepfather.

The two living brothers were age 28 and 25, both high school graduates and married with children. The elder brother was an insurance agent and the younger an auto mechanic.

The patient left high school after his second year to go to work, but later got his high school certificate in the Service. He worked at a gasoline station and a bowling alley prior to going into the Army. He served in the Paratroops from 1943 to 1945, was overseas in the Pacific, received a gunshot wound in his right knee, and was hospitalized for a 13-month period prior to his discharge. He married a girl whom he had known a short while when he was stationed in the South, but sent her back home after the war and divorced her. He had one child by his first wife, now in her custody. He met his present wife in 1946, a divorcee with a one-year old boy, and they were married a year later in December, 1947. He is Catholic and she is Protestant. The positive luetic history was mentioned previously. Except for a short period when he ran his own pickup and delivery cleaning business, he has worked since WWII at a cotton mill in various semi-skilled jobs.

According to his wife, the patient was a quiet, considerate, hardworking man. He was well-liked on his job and at the time of the onset of his present illness was being considered for a foreman's position. He was impatient, quick-tempered, and always quick in wanting to use his fists. His wife recalled four occasions when he lost his temper and got into a fight. On one occasion this was with a man who whistled at his wife, and on another with a man who told dirty jokes so that they were overheard by his wife and him. He was very fond of his stepson, but was strict and could not tolerate any childish misbehavior.

He always avoided doctors unless he had a serious injury that needed treatment. He did not like closed-in places such as theaters, and frequently felt the same way in church on Sundays. He was interested in all sports and liked to go dancing. He had friends, but only occasionally went out with the "boys". He was lonely when his wife met him, and she said he seemed happy to be married.

Physical examination

On admission to the Neurology Service, the patient was a well-developed, well-nourished white male, slow in action and thought. He appeared confused at times, and occasionally seemed to be hallucinating. However, he was oriented in all three spheres. He laughed inappropriately and seemed depressed. His attention span was poor. No delusions were obtained at this time.

His general physical examination was within normal limits. His neurological examination revealed no motor weakness, but the deep tendon reflexes were more active in the left arm and leg than on the right. There was an unsustained ankle clonus on the left but no pathological reflexes. Gait was normal, but the arm swing on the left was less than on the right. Coordination testing revealed ataxia in left heel-to-knee and finger-to-nose tests, and awkwardness in finger-to-thumb movements on the left. There were no gross sensory disturbances. Cranial nerves revealed that optic disks were hazy bilaterally. Pupils were round, unequal in size on one occasion, reacted well to light and convergence. Speech was slurred. The other cranial nerves were intact.

Laboratory findings

Blood studies for syphilis were four plus. Lumbar puncture on admission revealed normal pressure, 15 lymphocytes and 10 polymorphonuclear cells per cu. mm., total protein 110 mg.%, increased globulin, first zone colloidal gold curve, and four plus serology.

Psychological examination on admission

In the intellectual sphere, there was evidence of an acute, diffuse organic involvement which interfered with attention and recent memory. In spite of a lowered full scale IQ of 83, which was in the dull normal range, it was felt that the patient would again be capable of normal intellectual achievement once the acute state cleared.

The Rorschach reflected a regressed ego which was attempting to stabilize at a paranoid schizophrenic level. The depth of the regression was manifested by the presence of blatant sexual preoccupations and tenacious clinging to the periphery of situations in order to avoid further ego disintegration. Underlying the present state was evidence for a severe depression, which was warded off by heightened paranoid and obsessive mechanisms. Premorbidly, the patient was felt to be a severe, rigid, obsessive-compulsive person who saw the world in black and white terms, with consequent concern over matters of right and wrong, good and evil, etc.

Hospital course and treatment

The patient was treated with 600,000 units of aqueous penicillin daily for a total of 12 million units. His neurological status returned to normal within two months except for a hyperactive left patella reflex. Repeat lumbar puncture in 1954, two months after the course of penicillin, revealed 5 polymorphonuclear cells per cu. mm., total protein 36 mg.%, globulin normal, first zone colloidal gold curve, and serology four plus. Repeat lumbar puncture in 1955, a year and a half after the course of penicillin, revealed 7 lymphocytes per cu. mm., total protein 42 mg.%, globulin slightly increased, colloidal gold curve flat, serology four plus. His luetic infection has thus

been considered to be inactive since his course of penicillin.

His mental status became progressively worse, and he was transferred to the Closed Ward Psychiatric Service two weeks after admission. He was hallucinating in both visual and auditory spheres, expressed grandiose and paranoid delusions, and was in poor contact with reality. At times he was markedly agitated and subject to hostile outbursts in response to his hallucinations including throwing a cup of milk against the wall, smashing ping pong paddles against the window screens, and breaking a chair by kicking it.

Because of his continued psychotic behavior, he was started on a combination of insulin coma and electroshock therapy four months after admission. He received 35 deep insulin comas in four months and 15 electroshock treatments concurrently the first two months. During the course of this treatment, he was often uncooperative in eating and taking fluids, and had one or more insulin reactions daily which had to be terminated by gavage or IV glucose. After four months because he had shown no clinical improvement, his somatic treatment was discontinued.

Following a staff conference at which his case was presented, he was placed on sodium amytal p.o. in the morning on alternate days to depress his anxiety level and bring him into better contact with reality. The effect of this drug on the first day of medication was remarkable in improving his socialization. However, this effect quickly diminished, and after a period of time he appeared to be more disturbed on the days he got the drug than on those he did not. During this period he was seen in occasional interviews, but was withdrawn and preoccupied with his hallucinations so that only occasionally could he be reached verbally. During his disturbed period he was as agitated as in the past, but during calmer periods appeared in better contact with reality.

The patient was then seen in 30- to 50-minute interviews two to five times weekly for the next year and a half. These interviews took place for one period of six weeks with the patient in a wet sheet pack. At one point when the patient was very threatening in the interviews, he was placed on Serpasil without significant benefit, except to cause severe side reactions at a dosage level of 6 mg daily. These were marked conjunctival injection, shaking of the hands and staggering gait which disappeared when the medication was stopped. At various times the therapist did jigsaw puzzles with the patient, and played checkers and ping pong.

Clinically, he showed improvement primarily in his ability to socialize. He became more aware of the people around him and their reactions and was able to participate in such complicated interpersonal activities as playing baseball, basketball and volleyball, though he still spent a good deal of time by himself doing jigsaw puzzles and playing solitaire. Most of the time he hallucinated and was subject to occasional angry verbal outbursts, but he no longer had prolonged periods of agitation. His thinking became less paranoid and grandiose, though he continued to project his difficulties a great deal.

He was transferred to a state hospital two and a half years after admission.

Psychodynamics as seen in the interviews

The most prominent feature of this patient's psychosis was the almost complete separation of his good self from his bad self. The good self was a spiritual being who lived in the "aerion" or "this area of space", which was part of his psychotic ideational system. The good self was originally "the first man born, Captain J. Borden, President of the Borden Milk Company, Commander-in-Chief of the Borden Army and the FBI, President of the United States." Borden was a name he had used when doing some radio work in the Army and was a pseudonym his father had once used. Later he became "Father LaCross, brilliant angel and saint, thine blue heaven", who was also in part Diane LaCross. The good self had no brain, only a "clean mind". He had all the authority and strength, which he called "valor merit". The "film" of his life was clean, and his thoughts were part of the "Catholic oration". He was at one time the "big man Doctor" who had a "serum for every sickness", and was "never sick . . . never a mental patient." The good self was also Catholic as he was in reality.

The bad self was X, "Pill Ignorance", the patient who was mentally sick, had a "vest"

5′ 10″ tall (the patient's height), was "too filthy, ignorant and horrible" to be a part of the "clean vest", had "bad blood", had syphilis which was called "lower section of the body disease". The "Film" of his life was ignorant, and his thoughts were part of the "ignorant oration". He was responsible for everything bad, which included "reformatory, adoption, kidnap, orphanage, state prison, jail, and murder". The bad self was also Protestant as was his wife.

The good self was the person he consciously identified with. The bad self was not experienced as part of himself, but as a separate being whom he perceived in his visual and auditory hallucinations, and whom he projected into other people in his environment. His hallucinations were identified not only with different aspects of himself, but also with different people in his past and present. He talked about significant persons in his environment as if they existed both in reality and as persons in his psychotic world with another name. For example, he knew the head nurse by her real name and also by the name Diane LaCross. He knew the therapist by his real name, but usually called him "Pill Ignorance." The battle he was fighting in his mind was that of the good self against the bad self, which he termed "friend against friend". On occasion in interviews when he got angry, his identification with his good self and projection of his bad self momentarily became confused. On one occasion after hitting the therapist, he denied having done so, said he had hit himself.

The verbal battle carried on in his mind between his good self and his bad self absorbed much of his energy and attention. He utilized certain gestures, words and phrases to ward off bad thoughts in his mind. A good word protected him from a bad word, and these were occasionally used in juxtaposition. For example, the word "LaCross" protected him against his real name. Similarly with numbers, the number "zero" had a magical quality in that it cancelled bad words and numbers.

Many of the thoughts produced by this patient fell into a frame-work of fear and anxiety about loss and injury and, from a symbolic point of view, were probably highly sexualized. Such thoughts were expressed in a number of interviews but not in response to any specific verbal stimulus. For example, he said "You spend your life with a cup of coffee and a doughnut in front of you . . . every time your mouth touches a cup or a ring your tongue goes out . . . every time you open your mouth your tongue goes out automatically . . . every time you say that you lose your head automatically . . . cut off my neck every time . . . repeatedly . . . thine never touch . . . free hand on the neck . . . having supposed baby . . . I hate it . . . cut it off every time I see it." The fear about loss and injury was further underlined by his always talking about "sledgehammers, knives, and magic needles", and his saying on more than one occasion that "period" was the cause of all illness.

Certain things the patient said indicated the presence of underlying severe guilt and depressive feelings. He said, "you'll get solitary confinement forever", apparently meaning this was all he deserved. He said the therapist did not "deserve the M-A-N . . . never was a man born." He apparently was saying there "never was a man born" to deny his own feelings that he did not deserve to be called a man. The depressive feelings were also seen in his continual denial of illness, which was a central focus in therapy. He repeatedly said that the therapist was not a doctor, that "there was no need of a doctor in this area of space", by which he appeared to deny his feelings of needing a doctor.

Case Discussion

From a dynamic point of view, the patient appeared to have been premorbidly an extremely narcissistic person subject to poorly controlled hostile outbursts, and struggling against strong passive needs primarily by obsessive compulsive means. This pattern was still very apparent in his psychotic state. His masculine identification was a weak one with a father who was demanding, a strict disciplinarian, and undoubtedly quite threatening so that a satisfying relationship never developed. His two brothers were evidently closer to the father and made better identifications, particularly the older one who became an insurance agent. The brunt of the father's desertion fell on the patient as the oldest son when he was 15, not only in terms of having to take over the father's role of working and

being head of the house, but also in losing the masculine support he needed to emancipate himself from the mother. This problem is seen in his present identification with a good, all-powerful, spiritual Father LaCross in whom he must maintain faith. The bad threatening father, who he felt was responsible for his syphilis and mental illness and threatened injury in the sense of total destruction, was rejected and projected outside of him. The premorbid displacement of fear of the father on to doctors was now even more prominent, and their help rejected as unnecessary. On the other hand, the patient felt he deserved this horrible punishment for his hostile feelings towards the father. This was seen in his bad self deserving solitary confinement forever, not deserving to be called a man, and in the underlying depression which represented his aggression turned against himself.

Premorbidly, his feminine identification was indicated in part by his marriage to an attractive seductive divorcee with whom he identified so closely that he took her being whistled at and overhearing dirty jokes while in her presence as personal insults which he had to defend himself against physically. This was seen similarly in his defending his mother against the alcoholic stepfather. In his psychotic state, the feminine identification, as was the masculine, appeared to be split. Father LaCross was also in part Diane LaCross, and "Pill Ignorance" was associated with "period" as the cause of all illness.

Genetically, the most prominent feature here as in any psychosis was that of a deep regression of a large part of the patient's ego. This was highlighted by the grandiosity of his thinking, the omnipotence he felt he possessed, the illogical rage he experienced when he got angry, and the primitive type of projection he used.

Economically, a large part of his energies was taken up with warding off the disturbing thoughts and feelings which emerged into consciousness. His preoccupation with the conflict was determined by the extent to which he was threatened by the depressive thoughts and feelings concerning his illness.

Structurally, his illness can be looked at as a battle by his primitive and aggressive superego against his instinctual wishes which were poorly handled by an ego damaged by organic cortical involvement. The weakening of his ego was also manifested by the above-mentioned dissociative reaction as well as by the regression to a primitive level. This pathological solution enabled him to maintain the denial of an illness which was overwhelmingly painful to him, but at the expense of contact with reality.

Physiologically, his luetic infection was arrested. The extent of his brain damage was undetermined, though clinically, he did not appear to be impaired intellectually. It was not possible to re-test him psychologically due to his lack of cooperation.

The failure of somatic treatment with this patient was consistent with the experience of Tomlinson (5) who found the prognosis for improvement best in patients with a manic or catatonic picture and poorest in those with a paranoid or dementia picture. The failure of sodium amytal to be effective when given on a regular dosage schedule to a paretic patient was consistent with the experience of Wallerstein (6).

Theoretical Discussion

What kind of integrated picture can be made from the findings of this case and the previously mentioned psychodynamic theories? The syphilitic infection and resultant cortical damage initiate the psychosis, the makeup of which is consistent with the patient's premorbid personality. Because of the damage to his personality structure, the patient is no longer able to carry out repression effectively and is overwhelmed by his instinctual forces. Here damage to what Schilder termed the brain system responsible for certain previously enumerated functions is equated with Coriat's damage to the ego and superego. The patient experiences the functional mental impairment as an object loss and reacts to this by regressing to an earlier stage of psychic development. What Schilder called psychic dissolution is similar to what Hollos and Ferenczi and Coriat called regression in that apparently the functional impairment causes the ego to regress. The patient defends himself against the feeling of loss and the ensuing anxiety, guilt, and

depression by denial and projection. The reversibility of the psychosis is dependent upon the extent of the cortical damage.

Some narcissistic regression is characteristically seen with any physical illness, and psychotic states may be associated with acute diseases of organs other than the brain. Theoretically, the ego in these cases is deficient in available energy and therefore overwhelmed by instinctual forces because the energy is invested in the body. If the brain is considered from the same point of view as any other bodily organ, the reaction to the brain damage in paresis would be predicated to some degree on the psychological significance of the brain in each individual personality. This might account for some of the psychological reactions seen in this disease, including those which present primarily an affective picture and those which present primarily a schizophrenic picture. The organic features of the disease would then consist of the intellectual impairment, loss of integrative functions, and complex emotional impoverishment seen in patients with cortical damage of any etiology. The extent of the cortical damage in this sense would be a limiting factor in determining the patient's capacity to recover. Such a determination is difficult to assay as there would also be limiting factors determined by the previous personality structure and the particular psychological reaction to the disease. The psychosis of general paresis would then be essentially a functional psychosis initiated by a functional mental loss caused by organic cortical damage.

SUMMARY

A patient with the psychosis of general paresis, who was under psychological treatment for two and a half years, was presented, and some clinical features discussed. Previous theories were discussed which tried to account for the occurrence of the psychosis on an organic and psychodynamic basis. An explanation was presented which considered the psychosis as occurring because of the ego's loss of integrative functioning caused by organic damage to the cortex. The psychological reaction was said to be secondary to the painful awareness of a defective organ, and regression to a primitive state occurred to avoid a painful reality.

BIBLIOGRAPHY

1. Coriat, I. H.: A psychoanalytic interpretation of the mental symptoms of paresis. *Psychoanalyt. Rev., 32:* 253–262, 1945.
2. Hollos, S., and Ferenczi, S.: *Psychoanalysis and the Psychic Disorder of General Paresis.* New York: Nervous and Mental Disease Publishing Co., 1925.
3. Kenyon, V. B., Rapoport, D., and Lozoff, M.: Notes on Metrazol in general paresis: A psychosomatic study. *Psychiatry, 4:* 165–176, 1941.
4. Rapoport, D.: Chapter 25. In *Organization and Pathology of Thought.* New York: Columbia Univ. Press, 1951.
5. Tomlinson, P. J.: Insulin and electric therapy in general paresis. *Psychiatric Quart., 18:* 413–421, 1944.
6. Wallerstein, R. S.: Treatment of the psychosis of general paresis with combined sodium amytal and psychotherapy. *Psychiatry, 14:* 307–317, 1951.

12 GRAY STREET
CAMBRIDGE, MASSACHUSETTS

PSYCHOSOMATIC FACTORS IN "BLACK-OUT"[1]

ALBERT J. SILVERMAN, CAPTAIN, USAF(MC), SANFORD I. COHEN, CAPTAIN, USAF(MC), AND GEORGE D. ZUIDEMA, CAPTAIN, USAF(MC)

INTRODUCTION

Black-out is the phenomenon of temporary loss of vision occurring in pilots as they pull out of a steep dive or turn. This phenomenon may be duplicated and studied under controlled situations on the human centrifuge. In essence, it is the result of the forces of angular acceleration acting against the ability of the cardiovasculature to utilize physiologic compensatory mechanisms in maintaining the blood pressure at the head and eyes. Thus, exposure to positive G-forces tends to decrease the hydrostatic head of pressure in the uppermost parts of the body. Decreased peripheral vision occurs first, then loss of peripheral vision and dimming of central vision. As the cardiovasculature fails to maintain the necessary pressure at the head and eyes, more decompensation occurs, and complete loss of vision or black-out ensues. If the same G-forces continue to be maintained, the subject loses consciousness in a matter of seconds.

At the Aero Medical Laboratory, experiments have been under way to determine the parameters involved in G-tolerance. This interest and the facility of the human centrifuge at the laboratory resulted in the authors' hope that since this was a physiological response, emotional factors might in some way be implicated and worthy of study.

The inter- and intra-individual variations in tolerance to G-forces have been an enigma to aero-medical research for years. Workers in the field of acceleration have been at a loss to explain or predict a subject's ability to withstand high G-forces one day and his early decompensation the next day. Since a blacked-out or unconscious pilot may shortly be a dead pilot, the importance to the Air Force of work in this area is obvious.

However, in spite of a great deal of research, G-tolerance variations have in general not been explicable. The indictment of such factors as habitus (the long, skinny pilot, it was rumored, had poor ability to withstand G-forces), resting blood pressure levels and general physical condition led to low correlations (1, 12).

There was also a general feeling that the prestress state of pilots or subjects riding the human centrifuge influences their tolerance to G-stress. However, attempts to correlate many possible predisposing factors have not been met with marked success. Factors such as fatigue, hypoglycemia and other events making a person more sensitive to hypoxia have been implicated but not definitely related (15).

Variations in black-out level may be considerable among different subjects, some having in general high tolerance, and others low.

The day-to-day deviations from a subject's mean G-tolerance might be extreme or minimal, but in any case subjects identified as high, middle or low G-tolerance tend to remain in their groups.

PHYSIOLOGY OF BLACK-OUT

In order to assess the possibility of the influence of emotional factors in "G"-tolerance and "G"-tolerance variations, it is extremely important to understand the known physiology of the phenomenon. This will be reviewed briefly at this time.

One of the major factors identified as a determinant of the threshold of black-out has been the cardiovascular compensatory reflexes which are apparently activated immediately upon the onset of acceleration stress (3). These reflexes are activated by such events as decrease in carotid sinus pressure, emptying of the pulmonary veins and emptying of the veins of the heart (13). Reflexes, such as the sino-aortic, are then called into action. Impulses ascend to the pressor vasomotor center of the medulla, and an increase in blood pressure results. Within one or two seconds vasoconstrictive impulses may reach the peripheral vessels for an immediate pressor effect, and a delayed

[1] From the Stress and Fatigue and Acceleration Sections, Aero Medical Laboratory, Wright Air Development Center, Wright-Patterson Air Force Base, Ohio.

response may shortly occur due to the release of humoral factors.

Edelburg (4) has described that the rate of reflex adjustment varies considerably from subject to subject, and feels that this variability might contribute greatly to inter-individual G-tolerance differences.

The fact that maintenance of blood pressure through reflexes, causing among other things increased peripheral vasoconstriction, seemed to be a major parameter in tolerance to G-forces, led the authors to speculate that emotional factors might influence black-out levels, due to the effect of psychic events on cardiovascular reflex responsivity and associated vascular phenomena.

Method of Investigation

Once it had been determined that black-out was a phenomenon, the physiologic mechanisms of which could be quite vulnerable to affective influences, it seemed reasonable to embark on a course of study to determine grossly whether there were psychologic differences among subjects with differing G-tolerances.

Also important to evaluate was whether emotional changes seemed to correlate with intra-individual black-out variations. Thus, in order to establish the existence of and apparent importance of psychosomatic factors in this cardiovascular phenomenon, three methods of preliminary investigations were utilized.

a. *Interviews with pilots.* Fifteen pilots were interviewed in order to determine whether they had noticed differences in their ability to withstand G-forces. They were asked to present their ideas about these variations and to speculate why they occurred.

b. *Observation of and discussion with centrifuge panel subjects.* Panel subjects were coworkers and volunteers from the laboratory. This afforded a unique opportunity for frequent observation of behavior of these subjects. In addition, informal discussions were possible, which allowed the authors to make some assessments about the gross emotional state of subjects, and any pertinent associated life situations.

c. *Affect state diary.* Two subjects, particularly skilled in the expression of their feelings, were asked to keep a diary of the emotional state they were in, in association to repeated rides on the human centrifuge.

Results

a. *Interviews with pilots.* Of the fifteen pilots who were interviewed, ten were "jet" pilots who were frequently exposed to G-forces. The remaining five flew only propeller craft and were unable to cast any light on the problem since their exposures to centrifugal forces were rare.

Among those frequently exposed to G-forces, there was general agreement that when they were worried or preoccupied, their G-tolerance tended to be less. One man assumed that this meant he took less good care of himself when he was upset, and that the resultant physiological imbalance influenced his G-tolerance. The remainder of the men felt that somehow being worried or anxious made them more fatigued and hence more susceptible to black-out.

Five pilots reported that their G-tolerance appeared much higher when they were actually flying the aircraft, than when they were passengers. These men related this phenomenon to the fact that when flying the airplane, they were doing something, were in charge, in control and felt a mastery over the situation. When they were passengers, they felt trapped, often worried about the proficiency of the pilot, felt passive and the stress was completely out of their control.

b. *Centrifuge panel subjects.* Over a three-month period frequent observation of and discussion with centrifuge subjects suggested that those subjects who black-out consistently only at high G-forces had certain character traits and consistent affective spectra. They appeared to be outgoing individuals, often chronically hostile (either overt or suppressed), or those who felt that they could master the stress and be in complete control.

On the other hand, panel subjects blacking out at lower levels appeared more chronically anxious, and often more preoccupied with the possibility of bodily harm.

It was also noted that on occasion, angry outbursts among subjects were associated with rises in their tolerance, while intensified anxiety was associated with a lowered tolerance at that time.

Subject A: This 34-year-old female pilot has a high G-tolerance (always over 4.4 G). She is well organized, poised, and competitive. Although not hostile, she is very aggressive and bright. Her initial anxiety when facing new situations is high, but her ability to master these stresses decreases her tension level. She is able to channel her aggression in a socially acceptable way and is hence quite popular in the laboratory.

Subject B: This 26-year-old male airman has a high G-tolerance (always over 4.2 G). He is bright but immature, chronically hostile and belligerent. His terrific drive for approval keeps him on the run. Any criticism provokes a temper outburst. In turn, he is an extremely critical person, whose competitive efforts never subside.

Subject C: This 25-year-old male officer has a low G-tolerance (average 3.1 G). He is a chronically anxious person, but is effective and does a good job "when I get a kick in the pants, which I know I need all the time." He is tense and constantly worries about "satisfying everybody". His religiosity is associated with very high moral standards. His attempts to maintain these standards, and his inevitable failure results in periodic bouts of anxiety and self-incrimination.

Subject D: This 30-year-old male officer has a low G-tolerance (average 3.0 G). He is an insecure and chronically anxious person. Although he is a regular volunteer, he is still very frightened of the centrifuge. "I often look under the centrifuge to see if the machinery is intact. I worry because it might break and throw me out. . . . The stress of my cardiovascular system bothers me."

c. *Emotions and G-tolerance diarys.* Two subjects kept a diary of their feelings while periodically riding the centrifuge.

Subject E: This 30-year-old white male was studied over a two-year period. His initial average black-out level over a period of 6 months was between 4–4.4 G. This relatively high tolerance (when compared with the laboratory population) was associated with a period of high productivity in his professional field of biological research. He was receiving recognition for his scientific efforts and became known as an expert in his field. As time went on, his superior chose to give the subject more and more administrative responsibility. This finally took up so much time that the subject's productivity fell, and he became chronically anxious and depressed. He felt he was losing his scientific position, was not meeting his own standards, and was being superseded in the scientific world by those around him. Associated with this period of anxiety, depression and preoccupation, was a gradual lowering of his G-tolerance until his new average level was 3–3.4 G.

One day, just prior to a centrifuge ride, the subject was reminiscing about the "good old days" when he was "really a scientist". For a few minutes he actually "relived the pleasant affects associated with days gone by". On that day, he blacked-out at 4 G.

Following this episode his G-tolerance returned to the lower levels, and he finally left his position with the Air Force to join an Eastern University Staff.

Subject F: This 30-year-old white male was studied over a 12-month period. His initial G-tolerance average over a 5-month period was between 3–3.4 G. During this time the subject was preoccupied with personal problems including his struggle to learn new techniques and his apparent lack of acceptance by the laboratory group. He was also fearful of failing an important examination for which he was studying. His triumphant return to duty after taking (and passing!) the examination was associated with a black-out level of 3.8 G.

After remaining at this level for a time, his G-tolerance fell abruptly to lower levels. This was associated with his assuming charge of a research section, and his concomitant concern over whether the move would be a successful one. His black-out levels gradually increased, however, as he felt more comfortable in this new role. On one occasion a violent argument preceded a high G-tolerance. His G-tolerance appears now to be nearer 3.8 than 3 G, and in general this is felt to be related to his general air of greater comfort, aggressivity and control of the situation.

Discussion

If one examines the anecdotal evidence presented above, it becomes apparent that direction of aggressive expression appears to be associated with G-tolerance variations. Anxiety, depression, fear and loss of control appear related to lower black-out levels, while anger expressed, relatively low levels of anxiety, and sense of mastery or control seem identifiable with high G-levels.

Since these observations were made repeatedly and appeared very frequently, it seemed clear that a psychophysiological factor was operative in black-out. The authors next considered the possible psychophysiological mechanisms by which these affects could influence the physiological response.

Psychic elements may affect vascular and biochemical patterns through various means. The cerebral cortical system is associated with stimuli producing intellectual responses. The limbic system is thought to be associated with emotional or affective responses. Both cortical and limbic systems may be important. Emotional and intellectual responses could alter blood pressure responsivity by direct neurogenic activity mediated by the hypothalamus, medullary cardiovascular vasomotor center and autonomic nervous system. Also, stimulation of the adrenal medulla may accompany exposure to psychologic stress. The adrenal is

innervated by sympathetic fibers which can be selectively stimulated.

Some investigators believe that stimulation of different hypothalamic areas produces the selective release of adrenaline and noradrenaline from the adrenal medulla. Most workers attribute the majority of endogenous noradrenaline to be released at sympathetic neural endings.

Von Euler (5, 6) considers that adrenaline is released in response to (or associated with) emotional stimuli, particularly anxiety, but considers that noradrenaline elaboration is a response to hypotensive vascular stimuli.

Work by Funkenstein (8, 9) has indicated that different affect states are associated with specific vascular and biochemical responses. He was able to demonstrate that when an outward expression of anger occurred in experimental or life situations, blood pressure elevations and excessive noradrenaline-like activity occurred. On the other hand, anger directed toward the self, depression or anxiety was associated with hypotensive responses and adrenaline-like activity. The relating of these affective responses to biochemical changes and vascular responses is especially exciting in view of the demonstration by Folkow and Von Euler (7) that the specific hypothalamic center governing the selective release of adrenaline was almost identical with the fear-flight center described by Hess (14). Hypothalamic stimulation also evokes rage responses. Von Euler has discovered a noradrenaline center. The rage and noradrenaline centers as yet have not been related. However, it should be noted that Hess's rage center when stimulated causes an elevation of blood pressure. Whether the rage and noradrenaline center will eventually also prove to be identical, or whether as Von Euler believes, noradrenaline is primarily released in response to cardiovascular stresses remains to be seen. It is at least worthy of mention that noradrenaline might be released as a concomitant of the cardiovascular responses associated with the motoric expression of rage.

In this regard, it is interesting that Goodall, working with wild animals, was able to show that aggressive, attacking, non-fearful animals such as the lion, chronically show high noradrenaline levels, while fearful retreating animals like the rabbit reveal adrenaline excesses (10).

The facts just expressed appeared to bear very strongly on the problem area of cardiovascular responsivity to hypotensive stresses. Adrenaline can of course raise or lower blood pressure. The hypotensive tendency is due to the effect of peripheral vasodilatation. The hypertensive propensity is due to the familiar increase in pulse rate and stroke volume. Noradrenaline, on the other hand, causes an increase in blood pressure by its over-all vasoconstrictor effects.

The role of other hormones in response to stress will only be mentioned briefly. It is clear that via hypothalamic-pituitary impulses, the adrenal cortex and thyroid may be stimulated. Both adrenal mineral corticoids and thyroid may potentiate the effects of the catechol amines.

Thus, the work of Funkenstein in relating affects, biochemical changes and physiological responses, and the work of Hess, Von Euler and others in delineating possible neurophysiological correlates, stimulated the hope that some aspects of the psychophysiological mechanisms operative in black-out could be elucidated by a focused multi-disciplined research project.

Strong preliminary confirmation of the hypothesis came from the work of Goodall and Meehan (11), working in conjunction with the Aero Medical Laboratory, who investigated catechol amine levels in G-tolerance.

Noradrenaline as mentioned previously is generally accepted as the neurohormone of sympathetic nerves and, as such, is one of the main agents for maintaining vascular tone and producing vasoconstriction. It seems reasonable to assume that noradrenaline originates during gravitational stress from the sympathetic nerve endings in response to the vascular changes produced as part of the compensatory mechanisms activated.

The results indicated that subjects with high G-tolerance have higher noradrenaline levels during gravitational stress and also have higher base line levels than subjects with low G.

With all these facts in mind, it was speculated by the authors that emotional factors might influence G-tolerance in the following way:

If the subjects were overtly angry, aggressive

or were involved in active mastery of the stress, this would be associated with the release of noradrenaline. Thus, cardiovascular compensation to high G-forces would be improved because of the vasoconstrictive effect of noradrenaline.

On the other hand, if the subjects were anxious, this would be associated with increased elaboration of adrenaline. The peripheral vasodilatory effect of adrenaline would enhance blood pooling, and a lower G-tolerance would ensue.

It was felt that these affects and impulses were the significant emotional determinants influencing some of the biochemical and physiologic mechanisms responsible for variations in G-tolerance.

It is pertinent to the hypothesis that Von Euler (6) has already demonstrated that pilots had higher noradrenaline levels than airplane passengers. Passengers also revealed higher adrenaline levels than pilots.

This is felt to be meaningful because of the well-known motoric, and hence cardiovascular component of outward directed aggression as compared with anxiety and fear.

In some subjects, it was anticipated that rather definite patterns would be noted, while in others there would be more variability. It was felt that some persons would be able to handle aggression, express it, and not be prone to high levels of anxiety; while others might not be able to express any aggressivity and would be easily threatened and made anxious. The anxiety could be due to the threat of being aggressive or the threat of the stress itself. A third group would be one in which aggression might be felt and expressed at certain times but inhibited at other times. In these people, it was felt that the anxiety levels would vary considerably. It should be stated here that aggression is not conceived of as necessarily being synonymous with hostility. It includes the active pursuit of desired objects or events or the active removal of frustrating or unpleasant factors.

In this paper an attempt has been made to demonstrate the identification of a psychosomatic factor in black-out, and the development of a hypothesis which presents a possible mechanism of action. Other communications describe further early experiments by the authors which have been designed to explore the correctness of the theory (2, 16).

Summary

1. On the basis of observation of behavior and interviews, a psychosomatic factor appeared to be identified in tolerance to G-forces.

2. Aggressive feelings appeared related to increased tolerance, while anxiety was associated with lower black-out levels.

3. The possible relationship of these affects to adrenaline/noradrenaline levels and hence to G-tolerance is discussed.

BIBLIOGRAPHY

1. Cochran, L. B., Gard, P., and Nozworthy, M. E.: U. S. Naval Aviation Medicine Report MM 001 059.02.10, August, 1954.
2. Cohen, S. I., Silverman, A. J., and Zuidema, G.: Physiologic stress response evaluation with focused interviews. Arch. Psychiat., *76:* 670, 1956.
3. Edelburg, R., Henry, J. P., Maciolek, J. A., Salzman, E., and Zuidema, G. D.: Acceleration of Slow and Rapid Onset. *J. Aviat. Med., 27:* 6,482 1956.
4. Edelburg, R.: Reflex activity as a determinant of tolerance to acceleration. *J. Aviat. Med.*, 1956 (In press).
5. Euler, U. S. Von: Noradrenaline in hypotensive states and shock. *Lancet, 269:* 2,151–154, 1955.
6. Euler, U. S. Von: *Noradrenaline.* Springfield, Illinois: Charles C Thomas, 1956.
7. Folkow, B., and Euler, U. S. Von: Selective activation of noradrenaline and adrenaline from the suprarenal gland of the cat by hypothalamic stimulation. *Circ. Research, 2:* 191–195, 1954.
8. Funkenstein, D. H.: The physiology of fear and anger. *Scient. Am., 192:* 74, 1955.
9. Funkenstein, D. H., King, S. H., and Drolette, M.: The direction of anger during a laboratory stress inducing situation. *Psychom. Med., 16:* 404, 1954.
10. Goodall, McCh.: Studies of adrenaline and noradrenaline in mammalian heart and suprarenals. *Acta Physiol. Scand., Suppl., 24:* 85, 1951.
11. Goodall, Mc., and Meehan, J. P.: Correlation of "G" tolerance to urinary adrenaline and noradrenaline. Presented at Am. Phys. Soc. meeting Rochester, N. Y. Sept. 1956.
12. Gauer, O.: *German Aviation Medicine, World War II*, Vol. I, pp. 554–583. USAF Wash., D. C., 1950.
13. Henry, J. P., and Pearce, J.: Atrial Stretch Receptors. *J. Physiol., 131:* 572, 1956
14. Hess, W. R.: *Die Funktionelle organization des vegetativin nervous system.* Basil: Benne Schwabl, 1948.
15. Leverett, S.: Unpublished data.
16. Silverman, A. J., Cohen, S. I., and Zuidema, G. Psycho-physiological investigations in cardiovascular stress. *Am. J. Psychiat. 113:* 8, 1957.

A METHOD FOR DIFFERENTIAL DIAGNOSIS OF BRAIN DAMAGE IN ADOLESCENTS

G. ELIZABETH BRYAN AND MORONI H. BROWN

The present study was designed to further refine the ratio method for the detection of cerebral pathology as first described by Hewson. Since Hewson's original reports in 1949 (3) several studies, including two preliminary investigations by the writers, have indicated that ratios provided a more flexible, valid method than have other approaches such as Wechsler's "signs" or various types of scatter analysis.

Each of Hewson's ratios was composed of a different combination of Wechsler-Bellevue (W-B) weighted subtest scores. Although 13 ratios were presented, only 8 of them were used to give a summary diagnosis ("J" score) of either organic, normal, or neurotic. In this technique, there were two critical cut-off scores for each ratio. Generally speaking, a normal summary diagnosis resulted when all eight of the ratio scores fell between the two critical cut-off scores. A neurotic summary diagnosis resulted when one or more of the eight scores was below the lower critical cut-off score, and an organic summary diagnosis resulted when at least one of the eight scores was above the upper critical cut-off score.[1]

In one of the preliminary studies by the writers, Hewson's original ratios were applied to the subtest scores of 108 seventh grade retarded readers. Using Hewson's criteria, 69% of the males were classified as organic while the same percentage of the females were classified as neurotic. Since the "neurotic" and "organic" diagnostic categories represented two extremes of performance, it was clear that male and female subjects (at least among retarded readers) do not perform similarly on the W-B.

Later the Hewson ratios were applied to the subtest scores of 240 subjects of equal sex representation in the early adolescent, late adolescent, and early adult ranges. These subjects were drawn from a non-clinic and presumably normal population. Among them there was a high rate of false positive organic diagnosis which decreased from younger to older age groups and which was more pronounced for males than for females.

The age and sex differences in ratio scores for a presumably normal sample as well as the pronounced sex differences among the retarded readers indicated that the critical cut-off scores for each ratio should be adjusted on the basis of normative data for each sex at different age levels.

Subjects

Two hundred subjects were used in the present study. The control group consisted of 160 adolescents drawn from a public school population. In this group, 40 males and 40 females between 12 and 15 years made up a young adolescent group, and a late adolescent group was composed of 40 males and 40 females between 17 and 20 years. None of these subjects had been referred for any kind of psychological study.

The experimental group was composed of 40 adolescents who were suspected of having, or known to have, brain damage and whose medical records were accessible. The cumulative medical record of each of these subjects was reviewed by a neurologist, and each subject was placed in one of four categories according to the degree of neurological impairment. The first two categories had negative neurological diagnoses (no signs of residual neurological impairment) with either (a) suspected brain damage or (b) convulsive disorder. The other two categories had positive neurological diagnoses (neurological signs of residual impairment) with either (a) mild neurological impairment or (b) moderate to marked neurological impairment. These last two categories included the known organic subjects while the first two categories included subjects who were suspected of having brain damage on the basis of their symptoms or medical history but who had no demonstrable neurological impairment. The criterion for classification was

[1] The reader should refer to Hewson's articles (3) for a more precise description of the ratios.

a thorough neurological examination including clinical and laboratory tests.

Although most studies in this area have used subjects with selected kinds of organic diagnoses such as brain tumor of cerebral atrophy, and have excluded other diagnostic categories such as aphasia, no subject was excluded from the present study because of the type of symtoms he presented. It is important to stress that the degree of neurological impairment and not the etiology, nor the location, nor the diagnosis was the sole criterion for inclusion.

Method

The Wechsler-Bellevue Intelligence Scale, Form I, was administered to each subject, and ratios were computed using Hewson's weighted score combinations. As mentioned previously, Hewson used only eight ratios for summary diagnoses, and the other five ratios were considered to be useful auxiliary ratios but not adequate for diagnostic purposes. New ratios for the adolescent age ranges were established in the present study by including one of the five auxiliary ratios with the first eight ratios. The critical cut-off scores for these nine ratios were then adjusted so as to give the lowest possible number of organic diagnoses for the subjects who had positive neurological diagnoses. For each of these nine adolescent ratios there were four critical cut-off scores, one for each sex at each of the two age levels. All scores which exceeded the critical cut-off limit for the proper age and sex classification of a subject were considered to be organic, and all scores which were at or below the appropriate critical cut-off score were called non-organic. An organic score on any of the nine adolescent ratios gave a subject an organic summary diagnosis.

Since the present study was concerned only with the organic and non-organic classifications, Hewson's "neurotic" diagnostic category was not used.

Table 1 gives the weighted score combinations for each of the nine adolescent ratios and the critical cut-off scores for each sex in the young and late adolescent age ranges.

TABLE 1.—Adolescent Ratios and Their Critical Scores

Ratio	Weighted Score Combination	Critical Score*			
		F-Early Adoles.	F-Late Adoles.	M-Early Adoles.	M-Late Adoles.
I	PA and PC / A and D Sy	1.9	1.6	2.0	1.7
II	I and C / A	4.5	4.5	3.8	3.8
III	I and C / D Sp and D Sy	1.8	1.5	1.9	1.9
IV	I and C / PA and D Sy	1.5	1.5	1.9	1.4
V	I and C / D Sy	3.7	2.8	3.6	3.9
VI	I and C / D Sp and PA and D Sy	1.0	1.0	1.0	1.0
VII†	D Sp and D Sy / S and BD	.5–1.1	.5–1.2	.4–1.0	.5–1.3
VIII	C and PA / D Sy	3.7	2.8	5.0	3.6
IX	OA and BD / D Sp and S	1.8	1.4	1.7	1.6

* Ratio scores which are at or below the critical score are within the non-organic range.

† Ratio scores which are above or below the critical score interval are indicative of organic involvement.

Results

Ratios 3, 4, 6, 7, and C (Table 1) never gave organic diagnoses to any of the normal control subjects. The scores of a few of the normal control subjects which were extreme enough to fall into the organic category were so deviant that it is likely that they were not false positives. In some cases these extreme scores may have been indicative of neurological impairment which was not reported by the subject or known to the school. This is particularly likely to occur in the case of convulsive disorders where the symptoms are successfully controlled by medication.

The usefulness of the adolescent ratios as compared to Hewson's original ratios in differentiating adolescents with known or suspected brain damage from a normal control group is shown in tables 2 and 3. The last column of table 2 shows that with Hewson's ratios, 27% of the control group had organic diagnoses and 73% had non-organic diagnoses. When the adolescent ratios were used, only 8% of the control group had organic diagnoses and 92% had non-organic diagnoses.

Table 3 shows that both Hewson's and the adolescent ratios gave organic diagnoses to

TABLE 2.—PERCENTAGE OF ORGANIC AND NON-ORGANIC CLASSIFICATION FOR THE CONTROL GROUP USING HEWSON'S AND THE ADOLESCENT RATIOS (N = 160)

Classification and Ratio Method	Female (12.5–15.5 years)	Female (17.5–20.5 years)	Male (12.5–15.5 years)	Male (17.5–20.5 years)	Sample Mean Per Cent
Non-organic					
Adolescent....	92	90	92	95	92
Hewson.....	75	92	52	72	73
Organic					
Adolescent....	8	10	8	5	8
Hewson.....	25	8	48	28	27

TABLE 3.—PERCENTAGE OF ORGANIC DIAGNOSIS FOR AN ADOLESCENT GROUP WITH SUSPECTED AND KNOWN BRAIN DAMAGE (N = 40)

Ratio Method	Negative Neurologic Diagnosis*		Positive Neurologic Diagnosis*	
	Suspected	Epilepsy	Mild	Moderate to marked
Adolescent.....	38	67	100	100
Hewson.....	38	17	67	95

Note: "Organic" and "non-organic" in this table refer to the summary diagnosis according to the adolescent ratios.

* According to clinical neurological findings.

38% of the subjects who were suspected of having brain damage but for whom no signs of neurological impairment were found. Hewson's ratios gave organic diagnoses to 17% of the subjects who had convulsive disorders with no evidence of neurological impairment while the adolescent ratios gave organic diagnoses to 67% of this group. For the subjects having positive neurological diagnoses with mild neurological impairment, Hewson's ratios gave organic diagnoses to 67%. The adolescent ratios gave organic diagnoses to all subjects in this group. In the group with positive neurological diagnoses and moderate to marked neurological impairment, Hewson's ratios gave 95% of the subjects organic diagnoses, while 100% of the subjects were classified as organic by the adolescent ratios.

DISCUSSION

One of the reasons why the ratio method seems to be workable is that it does not depend on the assumption that there is any typical scatter pattern for organics. Heretofore, Wechsler's "sign" method and Mental Deterioration Index (5), as well as the various differential score techniques such as scatter from the mean or vocabulary scores, as used by Rapaport (4) and Babcock (1), have all assumed that certain subtests would remain stable while others would be more sensitive to impairment and drop substantially. Usually the verbal subtests have been reported to be the more stable, and the classical brain damage pattern has been low performance with high verbal scores.

Results such as these usually have come from studies made in Veterans Administration hospitals where the subjects were largely male veterans whose organic conditions developed during the adult years. Caution should be used in making inferences from such a select sample to the general population. The diagnostic category of organic brain damage is too often used without considering the age at which the condition appeared, how long it has been present, and particularly the current amount of residual impairment.

In contrast to the commonly reported organic pattern, a number of adolescents in the present study had superior performance scores. One such case was a 14-year-old boy who had been comatose for 68 days following a skull fracture eight years prior to testing. Some pieces of bone remained in his brain for more than two years before they were removed. After the accident the boy had right hemiparesis, except for his face, and slight right side atrophy. While he was right handed prior to the accident, he later learned to use his left hand satisfactorily. He also had to learn to walk and to talk again. His current problems centered around difficulty in school. He could not remember spatial patterns and found reading an impossible challenge. He had an excellent memory for verbal material but his responses were parrot-like. They reflected a lack of rationalization and judgment and depended heavily on the concreteness of his own personal experiences. His digit span weighted score was below his own mean, but he repeated five digits in reverse order and only four in forward order. On the performance tests he completed all of the object assembly problems easily and received credit on all but two block design problems. Although this case is a well-chosen

example, it is not an atypical one since in the present study 15 of the 40 experimental subjects had performance scores higher than verbal, and five of the subjects had equal scores or one point difference between the two scores.

When the 40 experimental subjects were classified according to the age of onset of their condition there was a trend for lower full scale IQ's to be associated with early brain injury. The subjects whose impairment was present at birth had a mean IQ of 62. The mean IQ of subjects having infant injuries was 66. Those whose condition developed between the ages of 3 to 10 years had a mean IQ of 71, while subjects whose neurological impairment developed between the ages of 10 and 20 years had a mean IQ of 85. The number of subjects in the study is too small to justify extensive generalizations. However, the observations are in agreement with Hebb's statement that "the level of intelligence test performance is a function of the concepts that a patient has already developed. Once developed, a concept is retained, despite brain damage that, if it had occurred earlier, would have prevented the (intellectual) development." (2, p. 2).

Apparently it is the variety of patterns in these ratios plus the allowances for age and sex differences which makes them useful in detecting organic conditions of many different types.

Summary

On the basis of age and sex differences, nine of the thirteen ratios originally presented by Hewson were modified and successfully used to differentiate organic and non-organic adolescent subjects.

Among the 160 control subjects (40 of each sex in a young and in a late adolescent age range), 92% had non-organic summary diagnoses according to the adolescent ratios. Hewson's original ratios yielded only 73% non-organic diagnoses for this group. Of the 40 experimental subjects, 100% of those who had positive neurological diagnoses had organic diagnoses according to the adolescent ratios. Only 80% of these subjects had organic diagnoses when Hewson's original ratios were used. In the group who showed no residual neurological impairment, 38% of those suspected of organicity had organic diagnoses according to both Hewson's and the adolescent ratios. In the remaining subjects who showed no residual neurological impairment but who had convulsive disorders, 67% had organic diagnoses according to the adolescent ratios while only 16% were classified as organic by Hewson's original ratios. Relationships between the present IQ and the age of the subject at the time of injury indicated that early injured subjects had lower IQ's than did later injured subjects.

Bibliography

1. Babcock, H., and Levy, L.: *The Revised Examination for the Measurement of Efficiency of Mental Functioning*. Chicago: C. H. Stoelting, 1942.
2. Hebb, D. O.: *The Organization of Behavior*. New York: John Wiley, 1949.
3. Hewson, L. R.: The Wechsler-Bellevue Scale and the Substitution Test as aids in neuropsychiatric diagnosis. *J. Nerv. & Ment. Dis., 109:* 158–183, 246–266, 1949.
4. Rapaport, D., Gill, M., and Schafer, R.: *Diagnostic Psychological Testing*, Vol. I. Chicago: Yearbook Publishers, 1945.
5. Wechsler, D.: *The Measurement of Adult Intelligence*, 3rd Ed. Baltimore: The Williams & Wilkins Co., 1944.

Dept. of Psychology
University of Utah
Salt Lake City, Utah

THE LAW OF INITIAL VALUE IN NEUROLOGY AND PSYCHIATRY

Facts and Problems[1]

JOSEPH WILDER, M.D.

When Eppinger and Hess (13) published their book on "Vagotonia" in 1910, this event was hailed as the beginning of a clinical neurology of the autonomic nervous system. Their experiments with adrenalin, atropin, pilocarpin seemed to prove that every individual has his own characteristic response to autonomic drugs which stigmatizes him as normal, vagotonic or sympathicotonic. This seemed like an obvious assumption.

Nevertheless, most of the subsequent investigators failed to confirm such regularity of response even in one and the same individual. Should we then assume that there is no rule at all or that even under optimally equal conditions we cannot predict the effect of such widely used drugs as atropin or adrenalin? Part of the answer was supplied by Wilder in 1930 (78, 79). Wilder used mainly series of experiments with atropin, adrenalin and pilocarpin on the same individuals; dosis, time, experimental conditions were standardized. The result of every experiment was expressed in a figure; this figure represented the average rise or fall of the function tested (pulse, blood pressure, etc.) per minute within one hour. Those figures could then be used statistically. The prevalent methods of using just the maxima or minima of change or the shapes of the curves obtained proved to be quite misleading.

The most important result of Wilder's (79) studies was the establishment of a definite relation between the level of the function at the start of the experiment and the outcome of the reaction. Wilder assumed that this relation applies in general to all physiologic functions and quoted many examples from various fields of medicine to illustrate his thesis. The latter was summarized in the "Law of Initial Value" which says:

Not only the intensity but also the direction of a response of a body function to any agent depend to a large degree on the initial level of that function at the start of the experiment. The higher this "initial level", the smaller is the response to function-raising, the greater is the response to function-depressing agents. At more extreme initial levels there is a progressive tendency to "no response" and to "paradoxic reactions", i.e., a reversal of the usual direction of the response. This rule holds true for 75–85 per cent of all experiments.

To appreciate this result, it is necessary to emphasize that most investigators do not take the initial levels into account at all. If they do, they operate usually with the tacit assumption that the opposite of our law is true: that, e.g., a hypertensive individual will respond to adrenalin with a higher rise in pressure than one who is normotensive.

Figure 1 brings three examples of the operation of the Law of Initial Value. We can see from figure 1 that the responses are higher where the initial values are lower and *vice versa*, and that they tend to become negative instead of positive with rising initial values. We shall not discuss here the typical exception with the lowest initial values.

Other illustrations collected by Wilder in his original articles referred to pituitary extracts; basal metabolism; metabolism of sugar, calcium, water; functions of the heart, uterus, pupils, sweat glands; the motor nerve, etc.

Wilder, Mandel and Pollak (80) demonstrated also the relative unimportance of the dosis of adrenalin as compared with the importance of the initial level: if a second dosis of adrenalin is given after the blood pressure had been raised by the first dosis, the reaction will be smaller and not greater. This observation has been confirmed by many authors.

To appraise quantitatively the importance of our Law, we must realize that even small differences in initial values definitely influence

[1] From the Department of Neurology and Neurosurgery, New York Medical College. Based on a paper read before the Schilder Society in New York, January 5, 1956.

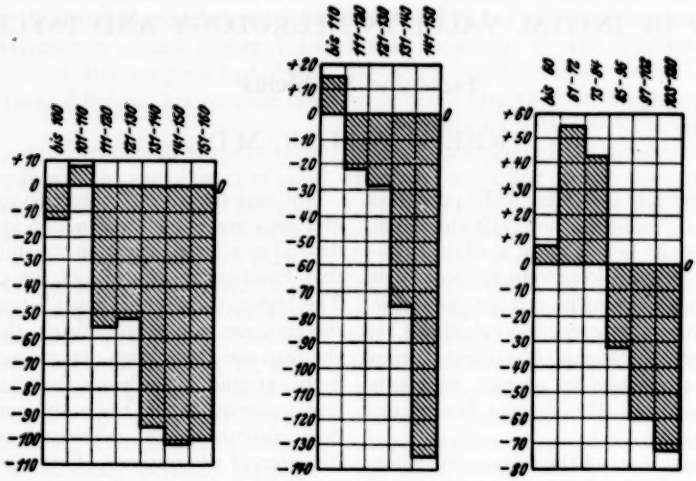


FIG. 1. From Wilder (79). Ordinate: The average change of blood pressure or pulse from initial value expressed in units of the surface enclosed by the basal line and the curve. Abscissa: groups of various initial levels. First graph: Blood pressure changes under atropin (78 tests). Second: Blood pressure changes under pilocarpin (16 tests). Third: Pulse rate changes under adrenalin (34 tests).

the response. This is linked to the fact that if the initial values are raised in arithmetical progression, the responses increase in logarithmic progression (68, 90) which is reminiscent of Weber-Fechner's psychophysical law. The tendency to paradoxic effect also increases in proportion to the rise in initial values (Wilder and Davies, 81). Attempts are being undertaken by various authors to work out a mathematical formula for this basic law.

The practical consequences of the acceptance of the Law of Initial Value, particularly in experimental medicine, are far reaching: 1) it should not be possible in the future to draw conclusions from experiments in which the initial values are not given and not properly taken into account; 2) two apparently equal responses are not equal if their initial values differ; 3) two apparently different responses may prove to be either equal or different if their initial values are properly considered; 4) apparently regular results may prove to be highly irregular; 5) apparently completely irregular results may show with consideration of their initial values beautiful regularity and yield important conclusions as has been emphasized by many authors (5, 17, 44, etc.). A critical revision of known experiments will show that their conclusions stand up to this criticism only if their initial values are known, if they are equal for all experiments, or if they are unequal, but the results run contrary to the expectations of our law. Unfortunately, these conditions are not fulfilled by the majority of experimental articles, and only recently have some authors stressed that their experiments pass the test of the Law of Initial Value which is at least as important as the establishment of proper controls.

We are still very far from the goal outlined here. Thus, e.g., a check of recent volumes of the famous "Archiv fuer experimentelle Pathologie" reveals that out of 131 relevant articles, 77 per cent do not state their initial values at all, and only 4.5 per cent take them into account. In recent volumes of "Psychosomatic Medicine" I find that out of 35 experimental articles, 57 per cent state their initial values fully, 17 per cent partly and 23 per cent not at all; only one article, however, takes those values into account.

Thus, the exact opposite of Eppinger and Hess' thesis is true: if a "sympathicotonic" individual has his usual high pulse rate at the start of the experiment, the tachycardic effect

of adrenalin will not be stronger but weaker than in the average individual. On the other hand, his response to inhibitors of the sympathetic system will be in such a state, not diminished but increased. These observations invalidate, e.g., much of the presently popular Funkenstein test which disregards differences in initial values.

Wilder and many later authors consider the Law of Initial Value as a basic biologic law. Some of the known quantitative general laws are only special cases of our law like the Weber-Fechner Law in the physiology of senses, the Arndt-Schultz Rule in the pharmacology, or Pflueger's Law of Electrotonus in neurophysiology.

Since its publication, the Law of Initial Value has been confirmed or applied by a rapidly increasing number of investigators, particularly in Germany, Switzerland and Russia. We can quote here but a few names out of several hundred: Fuss (17), Holtz (25), Leites (33), Mark (35), Mies (37, 38), Schimmler (48), Selbach (31, 44, 45, 54, 56), Spode (58, 59), Sturm (62, 63), Thedering (65, 66), Vieten (68, 69), Voelkel (70), Wezler (73, 74), Widmann (76), Ziolko (89), Zipf (90).

It is not surprising that all branches of medicine are represented: physiology (2, 33, 46, 48, 51, 55, 74), pharmacology (25, 90), endocrinology (14), internal medicine (10, 11, 62, 66, 67, 72), and especially cardiology (73, 74) and pneumatology (1, 28), surgery and especially neurosurgery (4, 15, 26), dermatology (42, 69), radiology (42, 47, 58, 59, 60, 68), physiotherapy (58, 59), balneology (49), sport and industrial medicine (37, 38, 71), etc. Among them, neurology and psychiatry are well represented, and it is one goal of this article to acquaint the reader with those recent developments.

The neuropsychiatrist will find that such hormones and transmitter substances as adrenalin (50 articles), acetylcholin (27 articles), insulin (17 articles), histamin and cortison act in accordance with the Law of Initial Value. He will find that a number of drugs which play a great role in neuropsychiatric research and treatment follow the same rule: strychnin, physostigmin, nicotin, ergotamin, novocain, atropin, papaverin, caffein, lobelin, phenobarbital, many narcotics, as well as iodine,

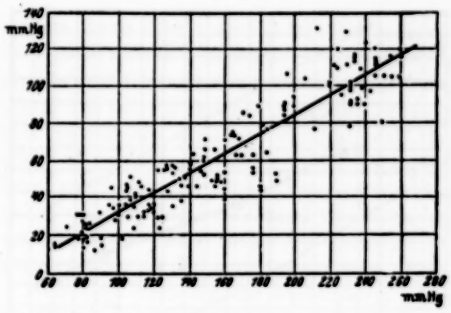


FIG. 2. From Zinnitz (88). Blood pressure drop in cats after intravenous injection of acetylcholin. Extent of drop (ordinate) as related to initial level (abscissa).

vitamins, iron salts, etc. Many authors emphasize the *precision* with which this law applies (e.g., Schimmler (48); see fig. 2 or fig. 8).

The psychosomaticist will note that for most functions of the body our law has been confirmed: for the muscle contraction, the gastrointestinal tract, the cardiovascular system (73, 74), for many phases of the metabolism (14, 33), for hematology (50, 76), dermatology (42, 69), for the effect of the x-ray (41, 47, 68), infrared and ultraviolet rays and even ordinary sunlight rays (58, 59, 60), on blood, skin, minerals, etc. They will learn that various effects of work, athletic activities (37, 38), vestibular stimulation, climate are subject to this law.

Most of our routine laboratory and testing procedures are affected by the Law of Initial Value and require specific precautions in its light. Thus, e.g., measurement of temperature changes in the extremities is often used by psychiatrists as a measure of excitement or anxiety. Figure 3 shows my own observations on the subject. We can see that the temperature of the foot rises or drops after the patient has uncovered his foot for 30 minutes, depending on its level while under the blanket, in accordance with our law. Within the narrow limits studied the room temperature proved to be of no significance.

Our figure 4 illustrates the dependence of serum iron on the initial value.

Figure 5 illustrates the dependence of blood leukocytes and their responses on the initial values.

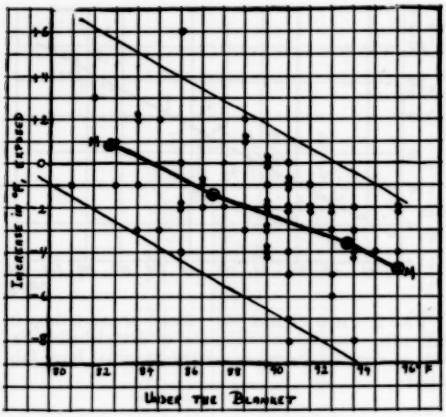


FIG. 3. Own experiments. Abscissa: initial level of temperature of the foot under the blanket in two patients. Ordinate: Rise (above zero) or drop (below zero) after ½ hour exposure to room temperature. There was no correlation with the slight variations of room temperature.

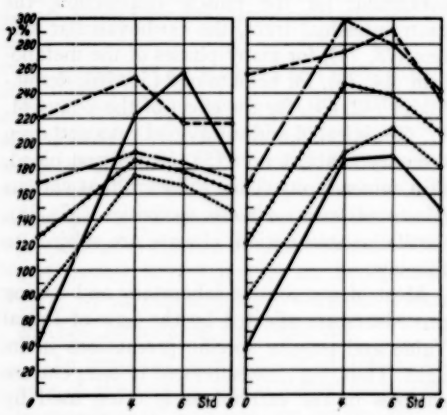


FIG. 4. From Thedering and Beck (67). Mean curves of serum iron in γ per cent after an oral dosis of 280 mg. iron. Time: 8 hours (abscissa). 5 groups of patients with various average initial levels of iron (ordinate). One hundred patients: left curves, men; right, women. Rise is related inversely to initial levels.

There is evidence that the effect of stress (Selye) which has attracted the attention of psychiatrists recently, depends on the initial value of the function studied. This seems to be true for eosinophilia (11), for 17-ketosteroids (47) and for capillary fragility which is considered an indication of stress (32). Thus, Voelkel (70) could show that under the effect of electroshock or of novocain this fragility rises if it was low at the start and drops if it was high.

Whitehorn (75), discussing the variety of responses to similar stresses in psychiatry, offers the explanation which is most popular among the psychosomaticists today: if in one case the gastric mucosa becomes red in a stressful situation and pale in another, this is due to the "difference in the *meaning* (italics ours) of stress to different persons under different circumstances and with different life experiences." This undoubtedly is true for certain cases. On the other hand, we have numerous observations to the effect that this response to stress will largely be determined by the degree of mucosal hyperemia at the moment of the experiment, regardless of its cause.

An easy self-experiment is to observe the reversal from a red dermographism to a white

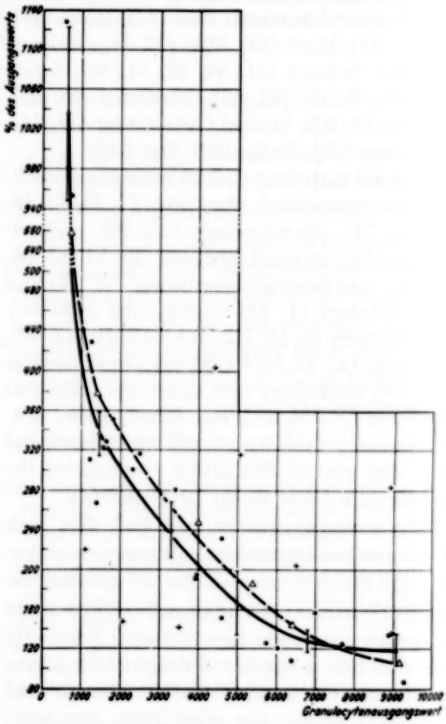


FIG. 5. From Widmann (76). Percentile changes in the number of granulocytes (ordinate) in 33 guinea pigs following prontosil and colchicin as related to the initial values of granulocytes (abscissa).

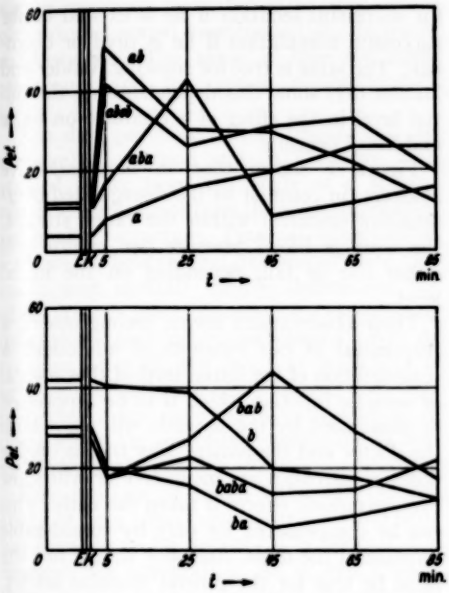


FIG. 6. From Voelkel (70). Ordinate: capillary fragility (number of petechiae) before and after electroshock (EK) during 85 minutes (abscissa). Upper group: low initial values; lower group: high initial values.

one in a skin hyperemic after a hot bath or exposure to sunlight.

The same relations as in our figure 6 obtain for numerous other effects of both the electroshock and novocain: blood sugar, pulse rate, blood pressure, caliber of capillaries, leukocytes, gastrointestinal motility, metabolism, etc. All these beautiful regularities remain concealed unless the Law of Initial Value is applied. Thus we can understand why novocain, which in large doses stimulates the central nervous system, nevertheless counteracts the tonic phase of the electroshock convulsion (61) as does benzedrine, etc.

Most of the experimental work in animals has been done with the use of *narcosis*. Narcosis interests also psychiatrists because of the possibility of well-dosed depression of psychic functions. It turns out that results of animal experiments under narcosis cannot be simply applied to the normal animal and, again, for a reason opposite to what we would customarily assume. All organs and especially the nervous system, up to a point, are not less but considerably more sensitive to stimuli under narcosis, and we often encounter paradoxical reactions. There are quite a number of studies proving this beyond any doubt. They deal with the effect of narcosis on the electrical responses, basal metabolism, the circulatory system, etc. (51, etc.). This has been found true even for respiration of plants under the influence of various narcotics and even for enzymes.

Most important are the experiments, e.g., by Thauer and Wezler (64), Rosenkoetter and Selbach (45) and others, demonstrating that additional doses of the same narcotic or addition of another narcotic at a certain point of the narcosis (a certain initial level) reverses the narcotic effect of the previous dosis. This reversal can be followed in various body functions. The phenomenon has also been followed in rabbits by electroencephalography.

The modern neurologist, thinking of narcosis, cannot ignore the reticular activating system (which is apparently also involved in the new "ataractics": Thorazine, Serpasil, etc.). There we have interesting studies by Caspers (9): electric pre-stimulation of this activating system does not hinder ether narcosis; on the contrary, it facilitates it. Only strong stimuli interfere with narcosis. The same is true for external stimuli so that perhaps a little noise in the operating room may facilitate narcosis. It may be that a little nervousness or fear facilitates it. In hyperthyroidism, for example, the basal metabolism often drops right before the operation.

The many paradoxical effects of the modern tranquillizers which often do not tranquillize but excite the patient, are no different from older observations about excitement following ingestion of bromides, phenobarbital, etc. There is a consensus of opinion that the ataractics act best with agitated, disturbed patients and have rarely any effect in quiet and depressed cases. The attempts to explain this phenomenon deal with the concepts of "individual susceptibility to drugs", the kind of disease process involved, or the "personality" of the patient. These explanations miss the obvious: that the effect depends to a great extent on the momentary mental condition of the patient at the time of the application of

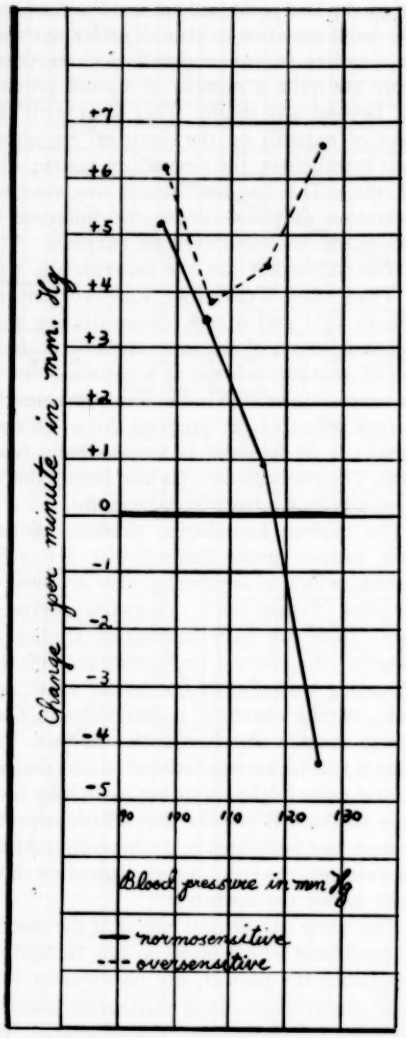


FIG. 7. From Wilder and Davies (81). Average rise in blood pressure per minute during 30 minutes (ordinate) after a cigarette in 5 groups of different initial levels (abscissa). Solid line: normoreactive smokers; broken line: clinically oversensitive smokers.

the drug. We come to similar conclusions if we observe the many paradoxic effects of ataractics in the somatic sphere. Thus, chlorpromazine may stop or cause nausea, depress or raise the temperature, etc. (Kinross-Wright (29) and others).

Everyday observation teaches us that the same "personality" may use a shot of whisky for successful sedation if he is excited or for successful stimulation if he is tired or downcast. The same is true for smoking. Wilder and Davies (81) show this dependence on the initial level in the effect of a cigarette on pulse and blood pressure.

Figure 7 shows that in normosensitive smokers (in contrast to the disregulated oversensitive smokers) within the range studied, the average blood pressure per minute will either rise or fall, depending on the initial level.

These observations invite, among others, a reappraisal of our concepts of addiction. A consideration of the initial level of that mental or somatic function which is to be suppressed or stimulated by the narcotic will show both the doctor and the patient why the successive doses of narcotics are ineffective or will show even paradoxic effects if taken too early. This can be compensated for only by considerable increase in the dosis. And why should not the same be true for the general stimulus addict, the sexual or mental stimulus addict?

These observations on the dual effect of sedatives were, of course, much easier to prove in the well-measurable somatic than in the elusive mental responses. There exists a considerable body of data to that effect. Especially the school of thought represented by the University of Rostock (Mark, 35), strong advocates of the Law of Initial Value, uses phenobarbital both as test and therapy in this sense. They speak of the "normalizing" effect of phenobarbital rather than of its sedative or stimulating effect.

What is true for the narcotics and sedatives is equally true for the *stimulants*. We have numerous clinical and experimental data to corroborate this in the case of adrenalin, benzedrin, pervitin, sympatol and their derivatives in their effect on the pupil, nictitating membrane (7), etc. In some of them, like the important nor-adrenalin, this effect is very weak in the normal organ but increases 20–30 times after denervation.

Twenty years ago, Misch (39) and Mayer-Gross (36) had already reported on the sedative effect of benzedrine and stressed its dependence on the Law of Initial Value. Nowadays benzedrine is widely used for sedation in restless and agitated children. Here the same drug, which night-club musicians use to keep themselves

awake, improves sleep; the same drug, which often causes sexual overstimulation, decreases masturbation. The same is true for other stimulants and for certain antihistaminics (23).

The dual psychotic effects (manic and depressive) of cortison and ACTH have been studied either from the angle of a specific effect on the brain or from the angle of previous personality structure. Personal observations lead me to believe that the initial state (somatic and mental) largely determines the effect. This is most important for establishing indications and contra-indications. We do consider, after all, the fact that digitalis acts only on the weakened heart muscle; that thyroid medication improves hypothyroidism in doses which are completely ineffective in normal individuals, etc.

How the Law of Initial Value can put the study of drug effects on a more scientific basis has been shown by Becker (3) in the case of a dexamyl-like preparation. As is well known, there are patients who complain that dexamyl makes them drowsy and others who feel overstimulated by this mixture of amytal and benzedrine. Becker writes: "The individual autonomic level proved to be the decisive criterion for the effect of the drug; Wilder's Rule of Initial Value in Selbach's modification could be fully confirmed."

Thus we begin to realize that there are two ways of sedation: by sedatives and by stimulants, both dependent on the initial state of stimulation or depression. Correspondingly there are two ways of stimulation. There are neurophysiologic data to support this. Thus, for example, Von Baumgarten and co-workers (2) have studied spikes from single cells of the reticular activating system in cats and their frequencies. When the cerebral cortex was stimulated, those frequencies either increased or decreased depending on their initial value: the low frequencies increased, the high decreased. A flash of light increases the low and decreases the high frequencies from a single fiber of the optic cortex.

Probably no drug has been studied so precisely in its "denervating" effect on the brain and mind as insulin has been. I am referring mainly to observations on normal people, self-experiments, accidental observations in diabetics and cases of spontaneous hypoglycemia. I have shown in my publications on this subject (83, 84 and others) many examples of this puzzling phenomenon: that only in the last stages of deep hypoglycemia are there lethargy, sopor and coma, and even here we often see an abundance of motor phenomena. But on the way down to that stage, in the mild and medium stages, as the electrical activity of the brain becomes less and less intense, we can see a whole gamut of psychic and psychomotor *productive* phenomena ranging from simple stubborn negativism down to almost every known psychotic and neurotic picture: paranoia, catatonia, melancholia, mania, hysteria, anxiety, obsession, epilepsy, etc. I never could see any relation to pre-psychotic personality other than in just any disease. I was satisfied many years ago to think of these active productions of the brain or mind in the accustomed way as "release phenomena", loss of inhibitions. Today I see in them partly symptoms of overreactivity of the brain to external and internal stimuli due to a lowered initial level, to denervation.

Before the Law of Initial Level the insulin effect, especially on the blood sugar, was considered as somewhat capricious. Let me show you the precision which it shows once the Law of Initial Value is applied to it.

Today the insulin test, provided the initial level is considered, is so precise that it is being used for brain diagnosis. We can now tell much better what is at a given level normal or ab-

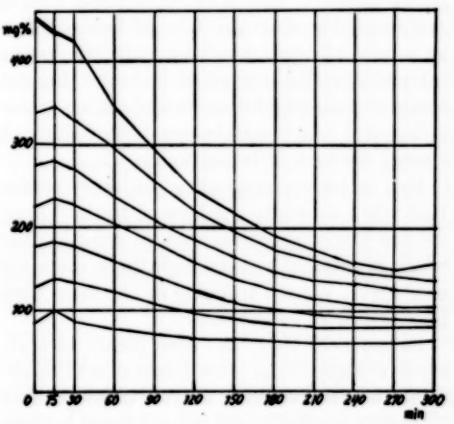


FIG. 8. From Mohnicke (40). Mean curves of insulin hypoglycemia during 5 hours (abscissa) as related to initial blood sugar levels. Ordinate: blood sugar levels.

normal. Disturbances, absent or unexpected paradoxic reactions, etc. are considered as a sign of mainly diencephalic lesion (57, 62, 63). This has reached such a point that in brain concussion an abnormal insulin test is considered by some as legal evidence even if subjective symptoms are absent. In combination with adrenalin and other tests it has contributed to the establishment of the group of "*diencephaloses*" which includes hyperthyroidism, diabetes, neuroses, etc. Sturm (62, 63) is the main proponent of this thesis which is hotly contested. Insulin tests in neuroses have been abandoned before because of their irregularity. Ziolko (89), with the help of the Law of Initial Value, found characteristic anomalies in 69 per cent of his neurotics. The insulin test also has been used for the investigation of constitutional types. It shows that the autonomic system is different in the leptosomic and the pycnic type. Winkler (87) says emphatically that the different insulin reactions are *not* due to the Law of Initial Value. Otherwise his results would be inconclusive.

Not only insulin, but other tests like sympatol, adrenalin, pituitrin, etc., in this new, improved version are being used as tools for the study of brain diseases. Autonomic abnormalities are thus found in epilepsy, cerebral arteriosclerosis, brain tumors, encephalitis, thallium poisoning, etc., as well as various neuroses. New terms like "hyporegulation", "hyperregulation", "regulatory ataxia", "regulatory rigidity" had to be introduced. This is not surprising since the Law of Initial Value is a principle governing not only the lowest intracellular bio-regulation but the highest forms of neuroregulation as well. Brain circulation and brain metabolism both follow, of course, the Law of Initial Value.

For better understanding we must realize that when we study the Law of Initial Value, we are studying phenomena of *refractoriness* which is growing parallel with the stimulation of a nerve. We are studying at the same time phenomena of *denervation*.

Before 1930 there has been plenty of scattered evidence that experimental results obtained on denervated or isolated organs cannot be simply applied to the intact animal because —and this was a puzzle—isolated or denervated organs do not react less but stronger to stimuli. I pointed out in 1930 how easily this can be fitted into the Law of Initial Value: as long as there is life at all in the tissue, there is *tonus* or better there is a low but constant state of excitation through stimuli which are largely unknown and which I summarily called "the stimulus of life." If this initial value of excitation is lowered by nerve section, every external exciting stimulus will produce an exaggerated and stronger reaction until the tissue dies (think, for example, of the electrical responses in Bell's palsy).

But there is not only surgical denervation. We have also the irreversible and reversible "chemical denervations". The classical example is the cocain block. I maintain that we are achieving various degrees of denervation by general anesthesias, by certain drugs and by such measures as lowering the sugar or the oxygen content of the brain or the peripheral nerve. It might even be permitted to ask whether there is any such thing as "psychic denervation". In all these cases, unless death or recovery of the nerve or the tissue takes place, we have a period of overexcitability of different duration and intensity. We can even determine the degree and the course of this denervation with almost mathematical precision by applying a given dosis of a stimulus at various moments (15). And yet, we are used to thinking in the wrong concepts: low nervous activity is automatically identified with lower excitability or with higher threshold.

Already in 1930, I linked Pflueger's Law of Electrotonus (the depression of excitability of the nerve at the cathode during excitation) with the Law of Initial Value. This phenomenon has been very well studied quantitatively by Lloyd (34) and others, on single spikes from single cells and nerve fibers with their after-potentials. During a part of this action potential near the peak of the spike (high initial value), there is complete lack of excitability; during the brief negative after-potential (low initial value), there is an increase; and during the following positive after-potential (higher initial value), again a diminished response to new stimuli. Similar examples can be found in the work of other neurophysiologists (12, 20, 21, 22).

Here we see the operation of our law on the microscopic scale of milliseconds and microvolts. On the other side (but not the end yet) of the scale are observations on various forms

of biological rhythms, especially the day and night rhythm. It has been demonstrated that serum iron, leukocytes and body temperature behave very much according to the Law of Initial Value: where they are low in the morning, they tend to rise toward the evening and *vice versa* in reverse proportion to the initial morning values (65, 72).

It does not take a philosophical mind to realize that all our responses to stimuli are in the form of waves, sometimes microscopic, sometimes very large ones, often in interference with each other, rising steeply or slowly and dying at various speeds, often in the form of muted oscillations (Selbach). This is true for the "brain wave", the heartbeat, the respiration, the brief effect of an intravenous sympatol, and the long one of the subcutaneous insulin injection, for the menstrual, the seasonal cycles, etc.

What interests us here is that parallel with the rising and falling of the excitation we observe the opposite: fall and rise in excitability. Excitability stops being a factor only where absolute rest exists, where the initial value is zero. It is highly questionable whether more but very brief moments of such "rest from life" exist in the living organisms. It seems, however, that there is a relatively low activity at "rest" in the central nervous system as compared with the constant day and night work of the autonomic nervous system. Correspondingly the Law of Initial Value seems to play a larger role in the latter. It may be that the achievement of comparative rest (low initial value) with its corresponding quicker and stronger reactions is the main secret of the superiority of the central nervous system.

As we approach again this central nervous system and with it the psyche, we are forced to admit that there is still no better measurable link established between mind and body than the psychophysical law of Weber-Fechner: if, for example, a surface is illuminated by 10 candles (high initial value), the addition of one candle will be hardly noticed; if it is brightened by only one candle (low initial value), the sensation following the addition of one candle will be marked. Weber-Fechner's Law does not pay attention though to reversal phenomena.

The critics of this law, like Walter Cannon (8), scoffed at its scientific value: every sensation is a unique phenomenon which cannot be measured and compared. Modern electrophysiologists like Granit (20) have shown, however, that the frequencies accompanying, e.g., the photic stimulation of the retina actually obey the Weber-Fechner Law. This law with its decrease of sensation accompanying the rise of the initial value is certainly only a special case of our law (some authors even speak incorrectly of the Wilder-Fechner law).

As far as the central nervous system is concerned, one of the most compelling thoughts is this: there exists obviously something else besides stimulation and inhibition. There are diminished or increased responses, absent responses and—most important of all—reversed responses due to higher or lower initial values. In several papers, Wilder (82, etc.) has shown, for instance, that painful muscular cramps arising in certain individuals from trivial stimuli are to be found associated with pronounced hypotonia of the muscles. This is neither a problem of abnormal stimuli nor of release of inhibition; here a low initial value of permanent stimulation (low tonus, "physiologic denervation"), e.g., at night, is responsible for exaggerated responses of the muscles to trivial stimuli. If—by analogy only—we transfer the same concepts to psychology, we might face a revival of the abandoned concepts of "irritable weakness" (neurasthenia); we might see that besides the "dynamics", the active struggle of forces like stimulation and inhibition, we shall have to consider somewhat more mechanical concepts of refractoriness associated with stimulation and of paradoxic reactions. The paradoxic reaction can be explained in various ways. Originally Wilder and many others considered this phenomenon as an effect of counter-regulation of nervous origin (neuroregulation) while the decrease of excitability with rising excitation was held to be a property of every cell (bio-regulation). More facts, however, are coming to light which make it probable that this "paradoxic reaction" is also a property of every cell. This comes to mind particularly as we study the reversals of the stream of sodium and potassium ions in the cell during and after stimulation. This does by no means exclude that entire organs or systems and in the last instance whole organisms function along the same line as the unicellular organism. We can

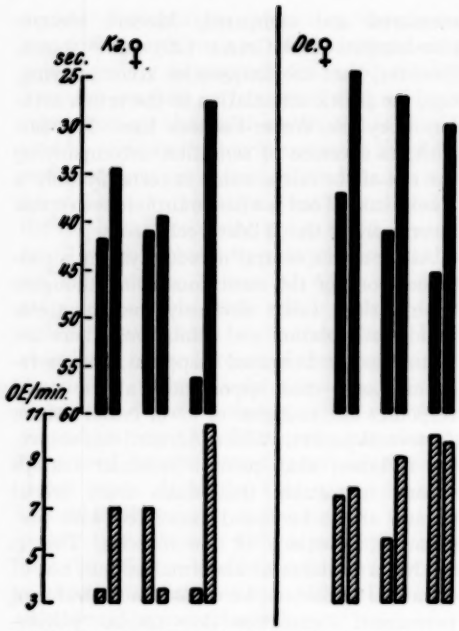


FIG. 9. From Mark (35). Motility of leukocytes after muscular work. Upper group (solid black): ordinate indicates number of changes of form per minute, lower group (striped): ordinate shows the distance the leukocytes wandered. First column of the pair: before; second column: after work. Two human subjects.

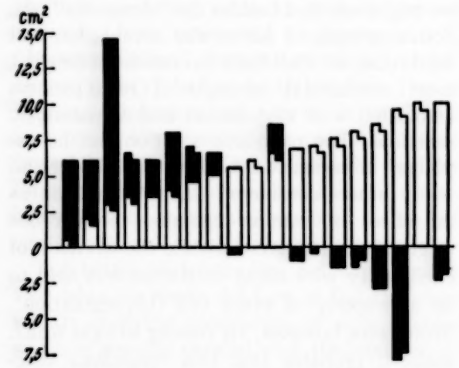


FIG. 10. From Wieser, Fetzner and Jordan (77). Abscissa: zero line for various cases. Ordinate: difference in the blood pressure after adrenalin expressed in cc.² of the surface enclosed between initial level and blood pressure curve. White: the reaction before electroshock. Black: increase above or decrease below the pre-shock reaction after electroshock in the same cases. Where the reactions were negative or weak before the shock, they tend to increase after the shock; where they were strong before, they tend to decrease after.

find the law operating even in fragments of cells (Selbach).

A neat example that the Law of Initial Value, including the reversal phenomenon, is a property of the cell can be seen in the studies by Seitz. Seitz (53) measured the motility of single leukocytes in the blood with the help of phase microscopy. Figure 9 shows some of his results.

We can see in figure 9 that the number of changes of shape per minute increases after muscular work in reverse proportion to the degree of such activity before work (black columns). Similar relations prevail if the distances are measured which the leukocytes cover by their movement (striped columns).

The mainly clinically oriented reader might be interested to learn more about some of the results obtained by application of the Law of the Initial Value in clinical research—results which could not have been obtained otherwise.

Thus the effect of electroshock still puzzles us greatly despite the excellent work done by Gellhorn (19) and others. Selbach in a number of articles (31, 44, 54) could throw a new light on this problem by using various tests and, particularly, the intravenous sympatol test before and, at various intervals, after the electric convulsions. His results can be roughly summarized as follows: the effect of the ECT on the autonomic system depends largely on the condition (tonus) of that system prior to the convulsions. Extreme parasympathetic (trophotropic) levels turn into sympathetic (ergotropic) and *vice versa*.

Selbach (54, 55) extended his studies and experiments to epilepsy and developed an entirely new theory of epilepsy based on the Law of Initial Value. According to him, epilepsy is mainly characterized by a deficiency in restoration of normal initial levels in a silent (lytic) way which forces the organism to seek restoration in the form of a crisis. Selbach says: The epileptic attack is identical with Wilder's paradoxic reaction. If the system is in a state of high tension, a minimal stimulus suffices to bring about a tilt (Selbach's tilt principle, 55). Klopp and Selbach's (31) investigation has been confirmed by many authors.

Figure 10 may serve as an illustration. It shows the change in the adrenalin response after electroshock (black) as compared with

the initial adrenalin response prior to the shoch (white). Where it was weak before, it becomes strong after the shock and *vice versa.*

Corresponding investigations by neurosurgeons dealing with brain concussion may throw unexpected sidelights on the entire problem of shock therapies. Fuss (17), Jensen (26) and others found the Law of Initial Value very useful in explaining many puzzles of sympathectomy (4) as well as those of brain concussion. Various pharmacodynamic tests were used before and after and various bodily changes were measured. It is fascinating to follow these investigations which show how regularly the effect of a brain concussion consists in the *reversal* of the pre-traumatic autonomic level. For example, where the leukocytes, blood sugar, blood pressure, etc., were high, there the concussion leads to a drop, where they were low to a rise. This is exactly what has been found by Selbach and many others in electric or metrazol shock. There is a potentially very important side observation of Fuss: exactly the same changes occur after injuries *in other parts of the body.* This reminds us of occasional remissions of melancholic depression after various injuries. In an interesting recent article, Jones and co-workers (27) report about favorable results in psychoses with *peripheral* strong electric stimulation applied to the leg.

One more new development out of many should be briefly mentioned. The application of the Law of Initial Value to the seemingly chaotic responses of various autonomic disorders plays an important role in a marked revival of the interest in these vaso-vegetative neuroses in Europe under a new name, "vegetative dystonia". Mark (35) and many of his pupils have written much on this subject. Hoff (24) reports that the diagnosis of "vegetative dystonia" has been made in no less than 40 per cent out of 72,000 cases in neuropsychiatric clinics in Vienna and in 18 per cent out of 128,000 in medical clinics. There is some discussion whether this is a post-war phenomenon and whether vegetative dystonia actually is a new syndrome.

As an example of direct application of the Law of Initial Value in therapy, we mention Dennemark (10) who is treating hypertension successfully with adrenalin.

As we approach the *psychological* field with the tool of our law, we encounter the well-known special difficulties. The Law of Initial Value deals with measurable quantities or, to be precise, with *publicly* measurable quantities. Our psychological research deals with quantities like pain, need, drive, etc., which are, in my opinion, measurable, often with even greater precision but only by a *private* measuring system, not accessible simultaneously to more than one observer. This is not fully acceptable in our present scientific blueprint. And yet, the basic pain-pleasure principle is described by Freud (16) in quantitative terms as increasing and decreasing tension, and Freud's hope has always been that by invention of some method of, for instance, measuring libido, psychoanalysis would be promoted to the rank of a truly scientific discipline.

I can see two ways in which the application of the Law of Initial Value could make a contribution toward that goal. In the first place, if the relation between response to stimuli and the initial value extends beyond sensation to other realms of the psyche, then the following would be true: we could deduce from the strength and direction of the response to a given stimulus what the initial level of the respective psychic function has been. Thus we could corroborate the patient's subjective statement. If the importance of the Initial Value for psychic functions is the same as for somatic functions, this corroboration has a probability value of 75–85 per cent.

Very few attempts have been made as yet in this direction, like C. and H. Selbach's (56) analysis of mental crises. Especially the effect of the "second stimulus", be it psychic or somatic, seems to follow our law. Gerhardt and Ziolko (18), using the Rorschach test, find a certain reverse relation to the pre-experimental psychic level after pervitin, etc.

The second contribution which our law is making to psychology already is in the area of "publicly measurable" somatic changes associated with psychic processes. There exists a tremendous experimental literature on that subject. It is often characterized by confusing and contradictory results. A survey of the literature on the effect of hypnotically induced emotions on various bodily functions would show this confusion best. It should interest

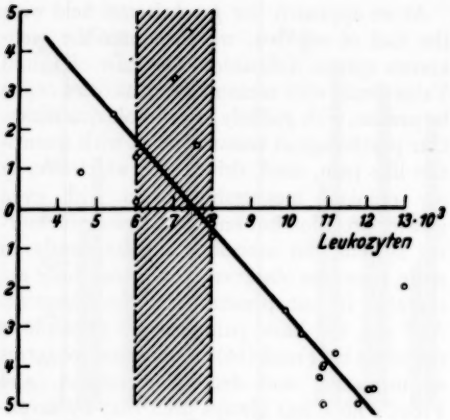


FIG. 11. From Kleinsorge (30). Rise above or drop below zero in the number of leukocytes (ordinate) in relation to the initial value of leukocytes (abscissa) following hypnotically suggested fear in 17 students (circles). Striped area: Normal range of initial values

the student of psychosomatic medicine that here too many contradictions resolve themselves promptly if the Law of Initial Value is applied. Kleinsorge (30) has shown this in interesting experiments on normal individuals. Figure 11 shows that the same emotion of fear will either raise or depress the number of blood leukocytes in inverse relation to their initial value.

The same is true for various other bodily functions. It is also true for repeated experiments in a single individual.

Thus it seems that the Law of Initial Value not only introduces important corrections into our scientific methods, but opens many new avenues of thought and research for the creative investigator.

SUMMARY

Our experimental work and our theoretical thinking are handicapped by the widespread disregard of the Law of Initial Value. This basic biologic law states that there is a specific inverse relation between the intensity and direction of a response to a stimulus, on one hand, and the pre-experimental level of a function tested on the other. A brief survey of the large but scattered literature on the subject is presented with special emphasis on neurology and psychiatry. A few indications of the many possible practical and theoretical applications are given.

After completion of this article we received a very interesting monograph by J. I. Lacey: The Evaluation of Autonomic Responses: toward a General Solution. The author treats the Law of Initial Value with superior statistical and mathematical methods, confirms it fully and realizes its general importance. The author works mainly in the field of psychosomatics (*Ann. New York Acad. Sc., 67:* 123, 1956).

BIBLIOGRAPHY

1. Bange, W.: Spontaneous pneumothorax and alveolar spasm, an autonomic problem. *Ärztl. Wchnschr., 7:* 224, 1952.
2. Baumgarten, R. von, Mollica, A., and Moruzzi: Modulations of frequencies of discharges from single cells of the reticular substance, etc. *Arch. ges. Physiol., 259:* 56, 1954.
3. Becker, W. F.: New ways of directed treatment of psychovegetative deviations. *Ärztl. Forsch., 8:* 528, 1954.
4. Block, W.: Phase of lability and stabilization of the autonomic nervous system after sympathetic surgery. *Arch. klin. Chir., 273:* 738, 1953.
5. Bodechtel, G.: Clinics of the autonomic nervous system. *Deutsches Arch. klin. Med., 195:* 57, 1949.
6. Boyd, L. J.: *The Simile in Medicine.* Philadelphia: Boericke and Tafel, 1936.
7. Burn, J. H.: Relation of motor and inhibitor effects of local hormones. *Physiol. Rev., 30:* 177, 1950.
8. Cannon, W. B.: *The Way of Investigator.* New York: W. W. Norton & Co., 1945.
9. Caspers, H.: Stimulation and inhibition of narcotic effects on the central nervous system, etc. *Ztschr. ges. exper. Med., 125:* 386, 1955.
10. Dennemark, H. G.: Hypertension and adrenalin. *Therap. Gegenw., 90:* 257, 1951.
11. Dittmar, F.: The necessity and possibility of an autonomic therapy of internal diseases. *Ztschr. ges. inn. Med., 5:* 489, 1950.
12. Eccles, J. C.: *The Neurophysiological Basis of Mind.* Oxford: Clarendon Press, 1953.
13. Eppinger, H., and Hess, L.: Vagotonia. *J. Nerv. & Ment. Dis.*, Public. Ser. No. 22, 1915.
14. Exner, R.: *Textbook of the Spirometric Analysis and Diagnosis.* Vienna: W. Maudrich, 1948.
15. Fleckenstein, A., and Bass, H.: The mechanism of reinforcement and weakening of the effect of sympathicomimetic amins by cocain and other drugs. *Arch. exper. Path. u. Pharmakol., 220:* 143, 1953.
16. Freud, S.: *An Outline of Psychoanalysis.* New York: W. W. Norton & Co., 1949.
17. Fuss, H.: Autonomic disturbances in commotio. *Ärztl Wchnschr., 9:* 586, 1954.
18. Gerhardt, U., and Ziolko, H. U.: The effect of pervitin in the Rorschach Test in neurotic women. *Arch. Psychiat., 192:* 311, 1954.
19. Gellhorn, E.: *Autonomic Regulations.* New York: Inter-science Publ., 1943.
20. Granit, R.: *Receptors and Sensory Perception.* New Haven: Yale University Press, 1955.
21. Hill, A. V.: Excitation and accommodation. *Proc. Roy. Soc. London, s. B., 119:* 305, 1936.
22. Hodgkin, A. L., and Huxley, A. F.: Resting and action potentials in single nervous fibres. *J. Physiol., 104:* 171, 1945.
23. Hoehnke, E.: Psychic-vegetative (retuning) effects of some s.c. antihistaminics. *Nervenarzt, 24:* 448, 1953.

24. Hoff, H.: The vegetative dystonia a disease entity? *Verhandl. deutsche. Gesellsch. inn. Med., 59:* 26, 1953.
25. Holtz, P.: The significance of the initial level for therapy. *Jahrb. ärztl. Fortbldg., 3:* 1, 1953.
26. Jensen, H. P.: Autonomic function tests for evaluation of post-concussional complaints. *Ärztl. Wchnschr., 9:* 800, 1954.
27. Jones, C. H., Shanklin, J. G., *et al.*: Peripheral electrical stimulation, a new form of psychiatric treatment. *Dis. Nerv. System., 16:* 323, 1955.
28. Kehler, E.: Basic neurovegetative problems of the muscular and vascular systems of the lungs. *Ärztl. Wchnschr., 7:* 197, 1953.
29. Kinross-Wright, V.: Complications of chlorpromazine treatment. *Dis. Nerv. System., 16:* 114, 1955.
30. Kleinsorge, H.: Psychologically caused regulations of leucocytes and their relation to Wilder's "Law of Initial Value". *Nervenarzt, 22:* 264, 1951.
31. Klopp, H. W., and Selbach, H.: The validity of the Rule of Initial Value in the epileptic. *Deutsche. Ztschr. Nervenh., 167:* 130, 1951.
32. Kramar, J., Peetz, D. J., and McCarthy, H. H.: Capillary response to emotions. *Psychosom. Med., 16:* 393, 1954.
33. Leites, S.: The Initial State Principle and its importance in physiology and pathology. *Lancet,* p. 1348 and Editorial p. 1364, 1936.
34. Lloyd, D. P. C.: In Fulton's *Textbook of Physiology.* Philadelphia: W. B. Saunders Co., 1955.
35. Mark, R. E.: *The Clinic of Vegetative Dystonia* Vienna: Springer, 1955.
36. Mayer-Gross, W.: Irritability as a symptom in manic-depressives. *J. Ment. Sc., 83:* 61, 1937.
37. Mies, H.: Investigations on the vegetative retuning during training. *Acta neuroveg., 8:* 149, 1953.
38. Mies, H.: Vestibular stimulation as tolerance test of the organism, etc. *Ztschr. ges. inn. Med., 2:* 520, 1947.
39. Misch, W.: The syndrom of neurotic anxiety: the somatic and psychic components of its genesis and therapy. *J. Ment. Sc., 81:* 389, 1935.
40. Mohnicke, G.: The insulin effect in diabetics in relation to time and initial blood sugar. *Ztschr. klin. Med., 149:* 574, 1952.
41. Pape, R.: Roentgen rays and autonomic system with special consideration of minimal doses. *Acta neuroveg., 3:* 474, 1952.
42. Pape, R., Brantner, K., and Jasky, K.: Control of early autonomic reactions following x-ray irradiation by the electrodermatography. *Strahlentherapie, 90:* 465, 1953.
43. Ploog, D.: Psychic counterregulation presented by the course of electro-convulsive therapy. *Arch. Psychiat, 183:* 617, 1950.
44. Ploog, D., and Selbach, H.: Functional reversal of the autonomic nervous system in the sympatol test during electroshock therapy. *Deutsche. Ztschr. Nervenh., 167:* 270, 1952.
45. Rosenkoetter, J., and Selbach, H.: The exciting effect of ethyl ether in evipan-narcosis in the electroencephalogram of the rabbit. *Klin. Wchnschr., 30:* 477, 1952.
46. Schaefer, H.: Basic problems of the autonomic tonic innervation. *Acta neuroveg., 4:* 201, 1952.
47. Schattmann, K., Schlungbaum, W., and Kuehne, P.: The influence of ionizing rays on the 17-ketosteroids and the number of eosinophiles. *Ärztl. Forsch., 9:* 342, 1955.
48. Schimmler, W.: The effect of intravenous novocain on arterial circulation and metabolism in man. *Arch. exper. Path. u. Pharmakol., 216:* 390, 1952.
49. Schoger, A.: Autonomic nervous system and spa therapy. *Deutsche med. Wchnschr., 75:* 506, 1950.
50. Schoog, M.: Critical considerations on Vaughan's leucopenic index. *Med. Klin., 45:* 1413, 1950.
51. Schroeder, W., and Anschuetz, F.: The effect of narcosis on the functioning of autonomic reflexes. *Ztschr. ges. exper. Med., 117:* 37, 1951.
52. Schroeder, W., and Anschuetz, F.: Investigations on the influence of the autonomic nervous system on the functional reactivity of the circulation in awake dogs. *Arch. ges. Physiol., 252:* 52, 1949.
53. Seitz, W.: Pharmacologic investigations on the effect of adrenalin and acetylcholin on living leucocytes in vegetative dystonia. *Folia haemat. 72:* 273, 1954.
54. Selbach, C., and Selbach, H.: Pathogenesis of the epileptic attack. *Fortschr. Neurol. Psychiat., 18:* 367, 1950.
55. Selbach, H.: The tilt principle in the analysis of vegetative autoregulation. *Fortschr. Neurol. Psychiat., 17:* 129, 1949.
56. Selbach, C., and Selbach, H.: Analysis of crisis. *Studium Generale, 9:* 394, 1956.
57. Simon, K.: Autonomic nervous system and blood sugar regulation. *Klin. Wchnschr., 28:* 152, 1950.
58. Spode, E.: New investigations on the influence of optic radiation on the bloodcells. *Arbeitstag. Biophysik,* Greifswald, p. 35, July 3–5, 1953.
59. Spode, E.: Investigation on the reaction of the blood to rays. I. Blood status in the rabbit as test for the ultraviolet effect. *Strahlentherapie, 93:* 15, 1954.
60. Spode, E.: The effect of the visible part of the spectrum on the peripheral blood cell count. *Naturwissenschaften, 41:* 21, 1954.
61. Stille, G.: The importance of centrally stimulating effects for the inhibition of the electroconvulsion *Arch. exper. Path. u. Pharmakol, 217:* 57, 1953.
62. Sturm, A.: The attitude of the internist toward the problem "hypothalamus and neurovegetative symptoms". *Schweiz. med. Wchnschr., 79:* 1099, 1949.
63. Sturm, A., and Wawersik, F.: Critical evaluation of autonomic function tests. *Med. Klin., 44:* 1281, 1949.
64. Thauer, R., and Wezler, K.: Circulatory effect of the commonest experimental narcotics. *Arch. exper. Path. u. Pharmakol., 200:* 84, 1942.
65. Thedering, F., Jr.: The importance of iron tolerance tests for the evaluation of the iron deficiency anemias. *Ztschr. ges. inn. Med., 3:* 547, 1948.
66. Thedering, F., Riethmueller, H. A., and Schwarzkopf, B.: Testing the fever capacity with pyrifer. *Ztschr. ges. inn. Med., 6:* 36, 1951.
67. Thedering, F., and Beck, R.: Disturbances of digestion and resorption of iron as pathogenetic factors in essential hypochromic anemia. *Klin. Wchnschr., 31:* 127, 1953.
68. Vieten, H.: The "Law of Initial Value" in the functional x-ray therapy. *Strahlentherapie, 78:* 429, 1949.
69. Vieten, H.: Law of Initial Value and roentgenerythema. *Strahlentherapie, 90:* 586, 1953.
70. Voelkel, A.: Changes in capillary fragility after electroconvulsion. *Klin. Wchnschr., 27:* 174, 1949.

71. Wachholder, K.: Need for and possibility of special care for nightworkers. *Deutsche Gesundh., 6:* 685, 1951.
72. Wagner, H., and Jordan, H.: Morning level and day periodicity as characteristics of the rhythm of body temperature. *Naturwissenschaften, 41:* 557, 1954.
73. Wezler, K.: The mechanics of circulation as basis of its neuro-hormonal regulation. *Wien. Arch. inn. Med., 37:* 226, 1943.
74. Wezler, K.: Autonomic regulations and retuning. *Arch. ges. Physiol., 244:* 622, 1941.
75. Whitehorn, J. C.: Stress and emotional health. *Am. J. Psychiat., 112:* 773, 1956.
76. Widmann, H.: Animal experiments on the relations of the leucocytic regulation to the "Law of Initial Value". *Klin. Wchnschr., 28:* 331, 1950.
77. Wieser, S., Fetzner, R., and Jordan, D.: Electroshock and vegetative integration. *Klin. Wchnschr., 31:* 314, 1953.
78. Wilder, J.: Pharmacotherapy and diagnostics of the autonomic nervous system. *Deutsche Ztschr. Nervenh., 116:* 194, 1930.
79. Wilder, J.: The "Law of Initial Value", a neglected biologic law and its importance for research and practice. *Ztschr. ges. Neurol. u. Psychiat., 137:* 317, 1931.
80. Wilder, J., Mandel, A., and Pollak, K.: Problems of the "Law of Initial Value". *Wien. Klin. Wchnschr., 4:* 1360, 1936.
81. Wilder, J., and Davies, H.: Cigaret smoking and the Law of Initial Value. (In print).
82. Wilder, J.: Crampus disease and localized muscular cramps. *Med. Record, 152:* 442, 1940.
83. Wilder, J.: *Clinic and Therapy of the Sugar Deficiency Sickness.* Vienna: Weidmann, 1936.
84. Wilder, J.: Sugar metabolism in its relation to criminology. In Lindner and Seliger: *Handbook of Correctional Medicine.* New York: Philosophical Library, 1945, p. 691.
85. Wilder, J.: Paradoxical reactions to treatment. *New York J. Med.* (In print).
86. Wilder, J.: Adrenalin in the light of the Law of Initial Value. *Exper. Med. & Surg.* (In print).
87. Winkler, W., and Froeschlin, W.: The insulin tolerance test. *Klin. Wchnschr., 28:* 617, 1950.
88. Zinnitz, F.: The relation of vagus effect and blood pressure by the action mechanism of acetylcholin. *Arch. exper. Path. u. Pharmakol., 188:* 329, 1937/8.
89. Ziolko, H. U.: Insulin tolerance tests in neurotic women. *Nervenarzt, 25:* 336, 1954.
90. Zipf, H. F.: Wilder's "Law of Initial Value". *Klin Wchnschr., 24/25:* 545 1947.

5 East 73rd Street
New York 21, N. Y.

MANIC DEPRESSIVE PSYCHOSIS: THEORY AND PRACTICE

G. M. DAVIDSON, M.D.

> Without theory practice is but routine born of habit. Theory alone can bring forth and develop the spirit of invention.
>
> *Louis Pasteur*

ORIENTATION

The significance of rhythm in human biology, such as the rhythms of pulse, respiration, menstruation, etc. is well established. One may even say that certain complex psychical phenomena such as our appreciation of "duration" are rooted in the individual's cognizance of biological rhythms. All human biological rhythms may be quickened or slowed in rate. It is also a fact that a biological rhythm has an affective component with a corresponding change in tone (heightened or decreased) concomitant with quickening and slowing of rhythm. Consequently, one may assume that the cognizance of the polarity of biological rhythm served as the background for the development of such psychical oppositional concepts as "good" and "bad", etc. It leads also to the possibility that affective (psychical) manifestations may give clues to concomitant physiological (biological) activity, as discussed by me elsewhere (10). It is my purpose to take up here the significance and relationship of the foregoing to the subject of the psychiatric disorder known as manic depressive psychosis. This seems particularly appropriate since in this disorder affectivity covers the whole horizon of the clinical picture as a *central* dominant phenomenon which may be maintained by the patient in a fairly uniform way (elation or depression) for an indefinite period of time. Observations of such mental states have been recorded since antiquity (think of the Bible personalities of *Nebuchadnezzar*, *Saul*, *Job*). In the less remote past the aforementioned states of affectivity have been spoken of as of "mania" and "melancholia", terms applied apparently to various states of *excitement* and *depression* irrespective of their nature. In more recent times we learned to differentiate these "opposites" better, but our knowledge of them is still incomplete.

Historically, while the conditions were noted earlier, Aretaeus of Cappadocia (200–300 A.D.) has described certain clinical manifestations of mania and melancholia surprisingly well. To quote Aretaeus in Jelliffe's translation: "... mania has intermittent periods and is curable. The form and ways which mania manifests are manifold. Some are cheerful and like to play, etc., others passionate and of destructive type. . . . As the disease begins to develop one notices passion, cheerfulness, or depression without cause, there is sleeplessness, headache, ringing in the ears, gluttony, or loss of appetite . . . at the height of the disease there is a loss of semen, and a period of lewdness, and shamelessness exists with the highest type of delirium. If there is a remission of the disease, the patient becomes quiet and depressed. . . ."

In more modern times, French psychiatrists Falret (15) in 1851 and Baillarger (3) in 1854 have noticed the circular character of the disorder. The latter writer emphasized that in *follie circulair* there are no two different states, but two different stages of one and the same attack which is a forerunner of our present attitude. Griesinger (19) in 1857 expressed the idea that in the majority of cases melancholia preceded the mania. Frequently during the whole course "the melancholia remains behind it as a shady background." I share this view since in my observation, there is always depression, no matter of how short a duration before manic excitement sets in. Moreover, I believe that depression may be still demonstrated in the background of a manic state. Kraepelin (23) in 1896 concluded that *mania*, *melancholia*, and *circular* reactions belong to the same process which he labeled *manic depressive* psychosis. He explained that one or another attack may occur in the course of life of the same individual and that the attack may repeat itself many times, but emphasized that the condition does not lead to deterioration. Periodicity is not fixed. While our present attitude toward the problem remains much the same, I would like to call attention to the following

clinical data and discuss certain theories and facts which may throw light on the nature of some, if not on all, of the said data.

The patient is usually of *pyknic* habitus and *cyclothymic* in makeup.

Both sexes may be subject to manic depressive psychosis, with preponderance of the female (up to 70 per cent).

Hereditary influence was considered by Kraepelin to range in his cases from 60 to 80 per cent. In recent times Rosanoff (31) has shown that 69.6 per cent of series of monozygotic twins develop manic depressive psychosis. It has been recorded also that the condition is more prevalent in certain groups of population than others.

The onset is acute or subacute. The average age of onset is between 15 and 25. In the state hospital about one-half of the cases of manic depressive psychosis are first admissions. The others are cases of readmission. The duration of the attack is between 4 to 6 months in the manic case and longer in the depressed case. The older the patient gets, the longer the attack may last. After middle life the incidence of depressed attacks is increased, apparently due to involution. The prognosis for the attack is usually good, but a few manic states may have a chronic course. Before the ECT era some cases of so-called "continuous excitement" had a fatal issue (13).

Symptomatology is well described in any text on psychiatry; therefore, I will omit its enumeration here. However, I would like to emphasize the necessity to approach the subject of symptomatology from the angle of "growth" or evolution of a symptom. Toward this end, I would like to point out that texts deal with pronounced cases of manic depressive psychosis, whereas in the general population there is a great number of personalities who manifest a mildly intensified rhythm of affectivity. Such personalities may be spoken of as of *cyclothyme*. The latter may be excellent companions or workers when on the "up-side", or may be difficult when on the "down-side". Still, their activities remain within limits of social tolerance, and they may or may not come for therapy. However, from the angle of "growth" of a symptom or syndrome *cyclothymia* must be considered as resting on the lower end of the scale which at its highest point reaches manic depressive psychosis. From the same angle of evolution both the manic and depressed phases have definite "growth" although not every case may demonstrate each step of the evolution. The reason for this is the fact that one or another step in the course of the growth may be overtaken by rapidity of development. To exemplify: the *depressed* phase may follow a progression from *simple retardation* to *acute depression* (sometimes erroneously called *acute melancholia*). I differentiate the latter as a complex affective state comprising depression, anxiety, remorse and nostalgia as discussed in (10), and to *stuporous depression*. The *manic* phase shows a corresponding progression of growth from *hypomania* to *acute mania* and to *delirious mania*. Further comments will be made later.

Next I would like to call particular attention to the *physical* aspects of manic depressive psychosis (a much neglected subject). To begin with attention is called to the fact that, while, as a rule, the patient is found in good general condition, he shows clinically a number of physical manifestations which deviate from his normal functioning. In the *manic* phase we observe an increase in pulse, temperature and respiration. The circulation time is increased; blood pressure and B.M.R. may be increased. The opposite may be found in the *depressed* phase. The depressed case may further show disturbances of the G.I. tract, such as coated tongue, constipation, and anorexia. In the female there is often amenorrhea (return of menses a favorable sign), and no sexual drive. In the male there is impotence.

McFarland and Goldstein (26) reviewed the blood-chemistry and found an increase in blood-sugar and high lipoid level in manic depressive cases. There is defective sugar tolerance in depression.

Tomasson (33, 34) gives interesting data on blood-electrolytes. He conducted daily estimates of blood-Ca and found correlation between the increased affective tone of depression, as observed clinically, with the increase of blood-Ca. He further found in states of apprehension—*hypersympaticotony*; in depression there were both *sympaticotony* and *vagotony*; there was *hypovagotony* in manic states; and *hyposympaticotony* and *hypervagotony* in severe depression. Since the *endocrines*, *sympathetic-parasympathetic* systems and *electrolytes* form a functional unit, it is reasonable to expect

repercussion of malfunctioning of a part of the unit in any other part of the unit. For instance, *erection* depends a good deal on parasympathetic activity on the physiological level. A decrease in activity of the latter will manifest itself in impotence. The influence of affectivity on the said unit will complicate the matter.

Neuropathology in manic depressive psychosis is given as negative. However, *functional* neuropathology is more than suspected, particularly on the levels of the hypothalamus, pituitary, and vegetative nuclei (from the angle of telencephalization of functions). Kubie (25) discussed the *instinct*-response to anticipation of danger by the individual. A good example appears to be the reaction of the Russian peasant to his cyclical needs toward the scarcity of food and work during the long Russian winters. The peasant increases his hours of sleep during the winter seasons. From the angle of "growth" the phenomenon is akin to the cyclical behavior of the animal in hibernation. Cushing and Goetsch (8) discussed the relationship of hibernation to adaptation to unfavorable conditions of life to the pituitary and hypothalamus. Cortical compensatory phenomena are also suspected.

Comments and Conclusions

Psychodynamics. The *depressed* phase is marked by preoccupation with death. This may be expressed in fear of death, in suicidal thought, in simulation of death as symbolized by the stuporous immobility and dream-like activity of seeing oneself in heaven, etc. (apparently psychic defense bringing about forgiveness). There are feelings of guilt which are the result of repressed hate; the latter being a rather prominent trait in the mechanism of depression. Other evidence points to anal and oral preoccupations, as may be judged from refusal of food, wetting and soiling, etc.

In the *manic* the central theme is referable to the idea of rebirth, or living out the life of another individual. There are exhibitionism and erotic attitudes of a childish character. There is also evidence of oral and anal interest, as demonstrated in biting, expectorating, obscenity, etc. Elation and grandiosity are equated with triumph of getting ones wish fulfilled.

Sexual freedom is sought in both phases as demonstrated in addition to erotic tendencies by the fact of denial of marriage, giving one's maiden name, etc.

The foregoing gross dynamics may be elaborated further psychoanalytically.

According to Freud (17), the depressed person has introjected and incorporated the lost love object. By doing so the patient identifies himself with it. He acts in response to either anticipation of loss of his love object (mild depression), or to an actual loss of his love object (severe depression). As Fenichel (16) puts it the patient is a "love addict" and is narcissistic. To exemplify, a patient of mine who was depressed dreamed of biting off the penis of her brother and swallowing it. She felt well after the dream. This is different from the "neurotic depression". For example, another patient of mine subject to a compulsive obsessive neurosis dreamed that she swallowed her wedding ring and that her husband found it in her elimination. In this case it is an attempt to force her husband to give her the affection she is seeking. The depressive mood continued.

Abraham (1) outlined the mechanism of the release of the depressive phase as follows:

A. A biological factor of inherited accentuation of oral erotism.

B. The fixation of the libido at the second oral stage when aggression is manifested in biting of the breast, etc.

C. A narcissistic injury sustained by the infant in early disappointment of live, especially by the mother before the Oedipus situation was overcome.

D. The repetition of primary disappointment in later life which serves as an exacting cause.

The foregoing may apply to a great number of cases.

Regarding elation, Freud's explanation is that the energy tied up in struggle between the *ego* and the *superego* is freed and is placed in the disposition of the *ego*, which now enjoys superabundant energy and indulges in triumph. Freud speculated also on a biological wisdom which makes differentiated parts of the total personality to coalesce periodically so that the part that arises later in development dissolves itself in its part of origin. Abraham compared the triumph of mania with celebration after mourning since it shows a good many features

of cannibalism just as depression does. However, I would like to point out that the freedom and triumph of the manic are not complete; there is still in the background hate; and oral manifestations are much in evidence. Considering the theory of introjections, the manic appears to seek continuously new objects for incorporation and ejaculation. Therefore, the assumption that the manic state follows the death of a hated parent is not applicable in all cases.

Rado (30) advanced the theory that the manic depressive cycle is to be identified with hunger and satiety of the infant, in which he sees a prototype of the condition. Depression or the threat of loss of love is equated with hunger; the earliest narcissistic bliss is seen in the satisfaction at the mother's breast. Depression is thus a desperate cry for love and expiation for guilt.

Jacobson (22) sees the mechanism of depression to lie in the fact that the patient could not develop a realistic relationship with the parents. Due to disappointment in the parents at an early Oedipus situation, the patient developed an overly strong *superego* by erecting within the personality the image of parent substitutes, idealized and perfect.

Bio- and *neurodynamics*. The foregoing survey of psychodynamics in manic depressive psychosis bears evidence to the interest shown by the researcher to the psychological level of the total personality in this psychiatric condition. On the other hand, the clinical material brings forward biological, somatic, and neurophysiological data which did not receive hitherto the attention that the findings merit. It is my intention, therefore, to discuss the significance of the findings and the possible relationship between the psychological and physiological data, even if admittedly in a speculative way.

At the outset of this writing attention was called to the significance of rhythm in biology and medicine, with particular reference to *total affectivity* in the sense of Kretschmer (24). Toward this end the findings and theories of Burridge (7) regarding the excitation process are of considerable interest. According to Burridge neurons are rhythmical tissues in a continuous state of activity. Excitation is, therefore, an act of addition rather than an act of striking as commonly assumed. Excitation has a psychological counterpart—*responsiveness*. The activities which evoke responsiveness are neural. The activities of the excitation process depend upon the combination of *colloidal aggregation* and *electrolytes*. Burridge denotes the former by the letter L and the latter by the letter H. L gives data for sensation and H supplies the emotional tone and judging capacity. The action of the two elements is synergic. The more there will be of L, the less of H, and *vice versa*. L plus H gives the factor T, which in turn denotes the capacity of the brain for *responsiveness*. In case L and H are maladjusted, uneasiness and agitation will occur. An overstimulation of L will result in shock. If the capacity of T is surpassed, there will be unconsciousness. Responsiveness may be augmented or diminished. There are two types of augmentation: the *rapid* and the *hysteresial*. The latter has the following chief properties: 1) The reaction outlasts the action of the evoker (after-effect), a phenomenon which explains *why* clinical symptoms may persist long after the cause which initiated them has long subsided. 2) Augmentation takes time to develop. 3) Augmentation shows marked capacity for summation. 4) It depends on adequate oxidation process. Of further interest is the fact that rhythms may be quickened or slowed. Again, there may be a change in amplitude of the excitation process; the greater the amplitude, the slower the response.

In applying the foregoing theory to emotional states, Burridge asserts that in depression we have a weakening of the factor L. As an adjustment there will be greater generation of the factor H. Through these changes plus slowing of their rhythms, the depressed patient reached the point of knowing self in a "highly disgusting way". Since colloidal systems have a property-lability which may be modified by drugs, hormones, traumas, emotions, etc., the probability allows to assume that increased colloidal lability may be a factor in *flight* of *ideas*, and a decreased lability may play a part in *slowed cerebration*.

Regarding the relationship of rhythmical activity to the vegetative nervous system, the sympathetic appears attuned to slowed rhythms, while the parasympathetic system is attuned to quickened rhythms (compare with data of Tomasson). The former is connected with mediation of fear, rage, etc.; the latter

will be associated with libidinous values. However, if the individual has connected sex ideas with disgust, it will become connected with the sympathetic system, but not the sex organs. The latter can only link with ideas that beat warmly; thus, reflecting on the nature of conflict.

Let us look now at the process of excitation from another angle. This brings us to the neurophysiological problem regarding central inhibition. One hears of a *monistic* and *dualistic* approach toward the problem. I prefer the *monistic* view for the following reasons: Lorente de Nó (14) observed that the central cortex consists of closed chains of neurons in a state of continuous activity (compare with Burridge), and that inhibition of one chain of neurons might involve inhibition of other chains of neurons. In addition, there are no known separate inhibitory and excitatory synapses. Pavlov (28) believes that cortical cells have two fundamental properties, namely *excitability* and *capability*. The cell has "top capability" (compare with factor T of Burridge), meaning if a stimulus reaches the top capability, the cell will react to such a stimulus with inhibition (this I believe does not happen when it surpasses its responsiveness as it may be assumed to be the case in "release"). I believe that the situation warrants the interpretation that inhibition may be regarded in certain instances as protective and defensive. It follows that in manic depressive psychosis the excitation process may work in the outlined way.

Regarding neurophysiological-psychological relationship one can speak of it at present in broad terms only. Keeping in mind the central mechanism of emotion in the sense of Papez (29) and the quoted data of Cushing and Goetsch, one may see depression as concomitant with dysfunction of subcortical levels and the manic state as a swing of the process to the cortical level with some retention of the original subcortical dysfunction. In psychological terms, the unconscious conflict (projected upon the subcortical level) is transformed into conscious *ego-penance* (compare with Burridge's observation on "becoming disgusted with oneself") with a swing to a triumph (rebirth, etc.). In the former there is a narrowing of consciousness upon oneself with a lowering of the ionic *milieu* (subcortical activity affecting cortical one). In the manic states there is the opposite, widening of the horizon of consciousness (distractibility, etc.) due to cortical excitement which subdues to a great extent but not altogether the subcortex. Therefore, one may see in the background of the manic state still some of the preceding depression.

Differential diagnosis. Texts on psychiatry differentiate in addition to the mentioned *manic*, *depressed*, and *circular* types, certain so-called *mixed* types, such as *agitated depression*, *manic stupor*, *unproductive mania*, etc. The diagnosis is usually made on the descriptive lines and by exclusion of schizophrenia. The follow-up of such cases, as shown in a former writing (13), proved the diagnosis in the investigated cases to be wrong because the usual approach has rather loose boundaries. Perhaps a step forward may be made by using my approach of the *final common path* of the *total personality* which I identified with *affectivity* as a coordinating mechanism (11). This method of study of psychiatric disorders is unbiased by the problem of etiology. For instance, the approach does not identify exclusively psychopathology with etiology, and furthermore allows for multiple causative factors. The approach is decidedly applicable to the present problem because it is *affectivity* which is the *central* clinical fact in the case under discussion. It is a fact that the patient maintains a uniformly heightened state of affectivity for an indefinite period of time until reduced to its prepsychotic level. In order to establish a clinical syndrome of manic depressive psychosis, I propose to aid the foregoing approach with the principles of Hughlings Jackson (21) regarding clinical symptomatology. Jackson differentiates: a) symptoms due to falling out of function of any kind, in part or as a whole, the result of injury of any kind (which are called "negative" symptoms); and b) symptoms due to "release from check" by impaired function (which are called "positive" symptoms). Attention is further called to symptoms which are due to efforts at reorganization of physiological and psychological mechanisms of unimpaired functions, which may also be present. Still another point is to evaluate the evolution or growth of a symptom (summarized in the section on orientation), for instance, the growth of *depression* to *stuporous depression*, meaning that the nature of the stupor in the said instance is rooted in the

evolution of depression. In such case the stupor will carry the earmarks of depression in contrast to a stupor, say of toxic nature, etc. It follows that the clinical syndrome of manic depressive psychosis consists exclusively of "positive" symptoms in contrast to schizophrenia in which the *primary* signs (in the sense of Bleuler) are identifiable with "negative" symptoms according to the present scheme. Since cases of manic depressive psychosis do not have "negative" symptoms which refer to withdrawal of affectivity, as discussed in a former writing (13), conditions such as *unproductive mania*, etc. are schizophrenic reactions. The cases of *agitated depression* do not belong either to manic depressive psychosis, even if they show only "positive" symptoms for the reason that such patients are strikingly different in their makeup from the *cyclothyms*. They offer obsessive compulsive traits in their temperamental makeup and morphologically lean toward the asthenic type. The affectivity is also of a different order, it leans toward melancholia (for details see (9)). From the same angle the diagnosis of *schizo-affective* psychosis is a misnomer. It is also for stated reasons that one may observe in the course of schizophrenia at times (in cross sections only) manic depressive symptomatology (due to defense forces of the personality), but no schizophrenic symptoms may be present in manic depressive psychosis. The foregoing is able to explain further why we do not have hallucinations or projection which may amount to a "trend" in manic depressive psychosis. Affectivity in the latter case is uniformly heightened. In the manic state it is uniformly triumphant. The flow is increased and is distractible; there is no possibility for isolation of thought to form an hallucination or a trend. One may observe occasionally an hallucination or a trend in *delirious mania*, but in such cases there is a toxic element present due to dehydration, etc. In some manic states one sees irritability, but the latter is also uniform in its expression (everything irritates the patient; no exclusive investment of affectivity in any one subject). In the depressed phase, affectivity is uniformly concentrated on the patient (somatic delusions, etc.)

The mechanism of "release". This is not known in all its detail. However, in a broad sense one may speak of the "release" as the result of failure of the hierarchical organization of the total personality. The failure is due to acute or continuous impact of stresses of all kind upon the individual, polarizing his maximum effort to respond (surpassing the factor T of Burridge or the "top capability" of the cell of Pavlov). The system of defense of the total personality will break down particularly the mechanism of repression, and compensation and overcompensation will seek to save the person's self-esteem. The cases for polarization of the maximum effort may be sought on the level of *mental conflict*, the telencephalization of the biological clash between constituents of *total affectivity* (in the sense of Kretschmer (24)), as discussed in a former writing (9) in which I have shown the disharmony of integration of various constituents of total affectivity in manic depressive psychosis. For instance, the discrepancy in integration between a strongly differentiated total affectivity and a diffuse, selective, insecure and frigid sex impulse. To exemplify clinically: A young man of 25, who was confused about his sexual-self since the age of 5 and who developed a strong homoerotic drive toward his father, attempted to solve his conflict since puberty by turning to religion. While in college studying to become a minister, he began to "doubt his relationship with God" and dropped his studies at the age of 22. He then developed a depression which was overtaken by a manic state. The attack repeated itself at 25 when a girl friend proposed marriage to him and a date of marriage was set. In each instance he ventilated his telencephalized biological conflict in harmony with foregoing observation on the nature of mental conflict. Another example is of a woman of 24 who had a strong Oedipus complex and strong ambitions, who was married unhappily and felt continuously frustrated. She developed a short depression followed by a manic state. The attack followed a dream in which she killed her mother. In the manic state she professed her eternal love for her father and promoted herself to her life long ambition of becoming a "star". These were typical cases. In each case a strong vulnerability of both the sympathetic and parasympathetic system was in evidence.

The influence of stresses may also affect the

physiological level of the totality, thus, ultimately causing a vicious cycle.

An interesting theory which may pertain to the mechanism of "release" is offered by Hebb. The theory is based on Humphrey's review (quoted by Hebb (20)) on "the problem of direction of thought". According to this theory (which is in harmony with other expressed ideas on the subject) any frequently repeated particular stimulation will lead to the slow development of a "cell-assembly", a diffuse structure comprising cells of the cortex and diencephalon (and also perhaps the basal ganglia), capable of acting briefly as a closed system and having a specific motor facilitation. A series of such events constitutes a "phase sequence"—the thought process (compare with "responsiveness" of Burridge). Each assembly action may be aroused by a preceding assembly, by a sensory event, or by both. This central organization is regarded essential to adult behavior. It is assumed that the assembly and organization depend on a delicate timing which might be disturbed by metabolic changes, as well as by sensory events. This will result in *disorganization*. If the latter is transient it may be called emotional disturbance; if chronic, neurosis or psychosis.

When the foregoing disorganization occurs, or when the factor T or "top capability" of the cell is surpassed, one could think that the total personality organization has reacted on the biochemical level in a state that Pascal and Davesne called "psychocolloidolclastic crisis" (27). These authors speak of a "psychocolloidolclastic diathesis". The latter is said to be marked by instability of mental, neurovegetative and colloidal equilibrium. The said characteristics are certainly found in subjects who develop manic depressive psychosis.

It is interesting to note that Pascal and Davesne considered that a psychocolloidolclastic diathesis does not have to be necessarily hereditary. This points to forcefulness of an individual experience. On the other hand, certain structures such as the neurovegetative may be hereditary and thus facilitate release. (The old argument of heredity vs. environment seems to have outlived itself.) Pascal and Davesne's approach may be of particular interest here since there is a reduction in frequency of occurrence of manic depressive psychosis in our times as compared with the times of Kraepelin, which requires explanation. One of the reasons for the reduction might be that our diagnostic criteria are better. But we must also be cognizant of the fact that the character of a disease process changes with times. In the latter cases physical (such as alimentary, climacteric, etc.), social, economic, etc. factors must be considered as instrumental in the change. For instance, Boas has already shown that the descendants of Slavonic brady-cephalic immigrants change in New York to dolichocephalios (5). Again, Shapiro has brought out the changes in descendants of Japanese immigrants in Hawaii (32). Bowles discussed "the new types of old Americans at Harvard and eastern women's colleges" (6). The mentioned factors, other than hereditary, may also explain why manic depressive psychosis may be prevalent in certain groups of population than others. In this category psychological factors, such as competitiveness, may play an outstanding role.

Regarding the prevalence of the female, texts bring out the fact that the generative phases of womanhood may contribute to it. This I believe is true; but in itself it cannot explain the whole situation. Perhaps more insight into this clinical fact may be obtained from better understanding of the experience of passing of the Oedipus complex by the female. I have discussed the nature of the "double allegiance" of the female to her parents which I assumed to be rooted in the biology of the X-chromosomes (12).

Therapy. Comparative studies of results of therapies of the past and present may be profitable for better understanding of the processes involved, as well as giving clues for research in the future. For instance, ECT therapy has shortened the course of an attack and has eliminated a fatal issue in certain cases of so-called "continuous excitement". We find the answer *why* in the workings of the therapy. According to Gellhorn (18) hypothalamic functioning is raised; it influences both the sympathetic and parasympathetic systems; it restores the autonomic balance; and influences the cortex itself. Now we know that at present ECT is the therapy of choice in depression particularly when accompanied by anxiety. The therapy is not as effective in manic states. It seems to me that the reason *why* it is rooted is the fact that the manic

state gives the patient a sense of well-being which he will not give up easy (compare with the alcoholist who will not give up drinking for even the briefest sense of satisfaction, taking the "hangover" in the bargain).

Regarding drug therapies, it is to be noted that Thorazine (2) which acts as a tranquillizer in schizophrenic type of excitement is not, as a rule, effective in manic depressive psychosis. On the other hand, Serpasil (4) seems more effective for the condition. It might be that Serpasil whose action is more selective toward depression of the central sympathetic function operates better than Thorazine whose action is more diffuse. The mechanism of the operation of the quoted therapies seems to fall in line with the discussed findings and theories of Burridge, Pavlov, Pascal and Davesne and Tomasson.

Needless to say that psychotherapy is most essential in any planned cure. Psychotherapy begins with the first meeting with the patient, must be followed up through the entire course of management of the treatment (in case psychotherapy is not *the* method), and continue after ECT is completed, as well as practiced along with and subsequently to pharmacotherapy.

Regarding preventive therapy, psychoanalysis, psychotherapy, ECT, and other methods did not prove efficient. But if psychical responsiveness, in the sense of Burridge, is rooted, as quoted, in our colloidal systems and ionic *milieu*, we must take care to maintain our two sources of energy in a most advantageous way. In other words, we must take care of our inner and outer environment. Our colloidal systems which give rise to sensation and help our adjustment in "space" (purposeful activity) are nourished to a great extent by the outer environment (which includes experience). This reflects on social, economic, alimentary, etc. factors. The ionic *milieu*, on the other hand, is chiefly influenced by inner forces, which reflects a good deal on affectivity, which in turn is tied up with the functional unit of endocrines, sympathetic-parasympathetic systems and electrolytes, and which is telencephalized to the thalamic and hypothalamic levels. It is in this direction that research in pharmacotherapy may prove promising with the ultimate goal to strengthen subcortico-cortical relay stations.

BIBLIOGRAPHY

1. Abraham, K.: *Selected Papers*. London: Hogarth Press, 1927.
2. Ayd, F. J., Jr.: The physiologic and neurologic action of chlorpromazine. *Psychiat. Research Report, 1:* 14, 1955.
3. Baillarger, J.: *Recherches sur les Maladies Mentales*. Paris: Masson, 1890.
4. Bein, von H. J., *et al.*: Experimentalle Untersuchungen über Serpasil (Reserpin). *Schweiz. med. Wchnschr., 83:* 1007, 1953.
5. Boas, F.: *Changes in Bodily Form of Descendants of Immigrants*. Washington, D. C.: Senate Documents, 1911.
6. Bowles, G. T.: *New Types of Old Americans at Harvard and Eastern Women's Colleges*. Harvard Univ. Press, Cambridge, 1932.
7. Burridge, W.: *A New Physiological Psychology*. London: Edward Arnold & Co., 1933.
8. Cushing, H., and Goetsch, E.: Hibernation and the pituitary body. *J. Exper. Med., 22:* 25, 1915.
9. Davidson, G. M.: Schizophrenia and manic depressive psychosis associated with pregnancy and childbirth. *Am. J. Psychiat., 92:* 1332, 1936.
10. Davidson, G. M.: The involutional (mental) syndrome. *Psychiatric Quart., 13:* 42, 1939.
11. Davidson, G. M.: The final common path of the total personality. *Psychiatric Quart., 18:* 459, 1945.
12. Davidson, G. M.: The biological aspects of the Oedipus complex. *Psychoanalyt. Rev., 42:* 280, 1955.
13. Davidson, G. M.: Schizophrenia: A survey of theory and practice. *J. Nerv. & Ment. Dis., 123:* 149, 1956.
14. De Nó, L.: Analysis of the activity of the chains of internuncial neurons. *J. Neurophysiol., 1:* 207, 1938.
15. Falret, J.: *Studies Cliniques sur les Maladies Mentales et Nerveus*. Paris: J. B. Baillieur, 1890.
16. Fenichel, O.: *The Psychoanalytic Theory of Neurosis*. New York: W. W. Norton Co., 1945.
17. Freud, S.: *Collected Papers*, Vol. IV. London: Hogarth Press, 1924.
18. Gellhorn, E.: *Autonomic Regulation*. New York: Interscience Publishers, 1943.
19. Griesinger, W.: *Mental Pathology and Therapeutics*. New York, 1862.
20. Hebb, D. O.: *Organization of Behavior*. New York: John Wiley & Sons, 1941.
21. Jackson, J. H.: *Selected Writings*. London: Hodder & Stoughton, 1932.
22. Jacobson, E.: Depression, the Oedipus complex in development of depressive mechanism. *Psychoanalyt. Quart., 12:* 511, 1943.
23. Kraepelin, E.: *Lehrbuch der Psychiatric*. Leipzig: J. A. Barth, 1896.
24. Kretschmer, E.: *Textbook of Medical Psychology*. New York: Oxford Univ. Press, 1934.
25. Kubie, L.: Instincts and homeostasis. *Psychosom. Med., 10:* 15, 1948.
26. McFarland, R. A., and Goldstein, H.: The biochemistry of manic depressive psychosis, A review. *Am. J. Psychiat., 96:* 21, 1934.
27. Pascal, C., and Davesne, J.: *Traitement des Maladies Mentales par les Chocs*. Paris: Masson, 1926.

28. Pavlov, I. P.: *Conditioned Reflexes and Psychiatry.* New York: International Publishers, 1941.
29. Papez, J. W.: A proposed mechanism of emotion. *Arch. Psychiat., 88:* 725, 1937.
30. Rado, S.: The problem of melancholia. *Internat. J. Psycho-Analysis, 9:* 134, 1928.
31. Rosanoff, A. J.: *Manual of Psychiatry.* New York: John Wiley & Sons, 1938.
32. Shapiro, H. L.: *Migration and Environment.* New York: Oxford Univ. Press, 1939.
33. Tomasson, H.: Medikamentöse Behandlung der Blutelektrolyten bei Manisch Depressiven Patienten. *Monatsschr. Psychiat. u. Neurol., 86:* 324, 1933.
34. Tomasson, H.: Therapeutic attempt in manic depressive psychosis. *J. Ment. Sc., 82:* 595, 1936.

MANHATTAN STATE HOSPITAL
WARD'S ISLAND, NEW YORK

TWO CASES OF INTRACRANIAL NEOPLASM TREATED BY CHEMOTHERAPY

SAMUEL ROSNER, M.D., F.I.C.S.

The purpose of this paper is to give a follow-up on a previously published case (11) and to add another case report of a patient treated by this method.

It is felt that this method may be applied to other cases of recurrent intracranial neoplasm which have not responded to the usual methods of attack. It is not the intention of the writer to propose that this method should be used in lieu of the standard methods. Rather, it is hoped that sufficient interest will be aroused so that this treatment will be tried where standard therapeutics have failed.

The routine of treatment is as follows: Two-tenths gm. of Bismarsen (donated by Abbott Lab.) and 5 gamma of Piromen (donated by Travenol Lab.), a bacterial polysaccharide diluted in 3 cc. of 2 per cent novocaine, are injected intramuscularly three times weekly for 20 injections. A rest period of four weeks is then given. Three courses of treatment are given with four weeks rest in between courses. After two months of rest, another three courses of treatment should be given as outlined above.

This method was used in the following case:

Case 1: F. L., female, white, age 47 years, was operated upon at Bellevue Hospital for a left temporoparietal meningioma, which was not completely removed. The left temporoparietal region was covered by muscle, but the bone flap had not been replaced.

Some months thereafter, the patient complained of recurrent headaches and pain in the incision. In May, 1948, craniotomy was performed because headache and vomiting could not be controlled by any medication and because the operative area began to bulge with increase in intracranial pressure. A great portion of the neoplasm was removed, and a tantalum plate was used to repair the defect.

The patient was comfortable until September, 1949, when she began having Jacksonian attacks, involving the right upper limb and face, recurrent headaches, bouts of vomiting and periods of disorientation. Operation was performed, and despite the extreme vascularity the greater part of the tumor was removed. The tantalum plate was not replaced. The patient was well with dilantin and phenobarbital. In the early part of January, 1953, Mrs. L. complained of headaches, vomiting, dizziness, frequent Jacksonian attacks, disorientation and violent attacks of temper without cause. Dilantin and phenobarbital no longer controlled the epileptic episodes.

The first injection was given on January 21, 1953. After the fifth injection she felt well. There were no headaches, no Jacksonian attacks, no loss of temper and no disorientation. After 12 injections the patient went on a 3-week vacation. During the last week of the vacation, Mrs. L. had a violent attack of temper tantrums followed by a Jacksonian attack.

On April 4, 1953, the injections were reinstituted. In May, 1953, the patient was involved in an automobile accident. That night she went into status epilepticus from which she recovered. In July, 1953, she had another epileptic attack. In August, 1953, she showed increase in proptosis of her left eye. Partial motor aphasia and proptosis had been present since the original operation in 1947.

On October 16, 1953, the injections were discontinued. On November 17, 1953, the patient had four epileptic attacks within two days. The patient was put on another course of treatment which was repeated after one month of rest. She was still taking dilantin and phenobarbital daily. There had been no convulsive seizures, no temper tantrums, no disorientation, and no headaches for six months following the last course of injections. The proptosis had diminished somewhat and speech had improved. Mrs. L. had gained weight and felt and looked well. There was a depression at the site of operation, and there had been no sign of increase in intracranial pressure since the last course of injections was finished in April, 1954.

In Jan., 1955, the patient had a major epi-

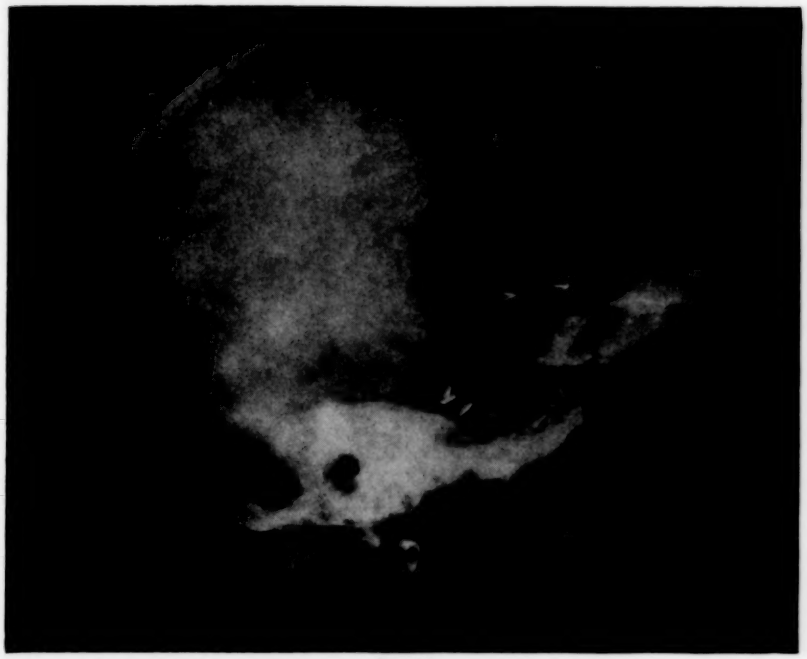


FIG. 1A

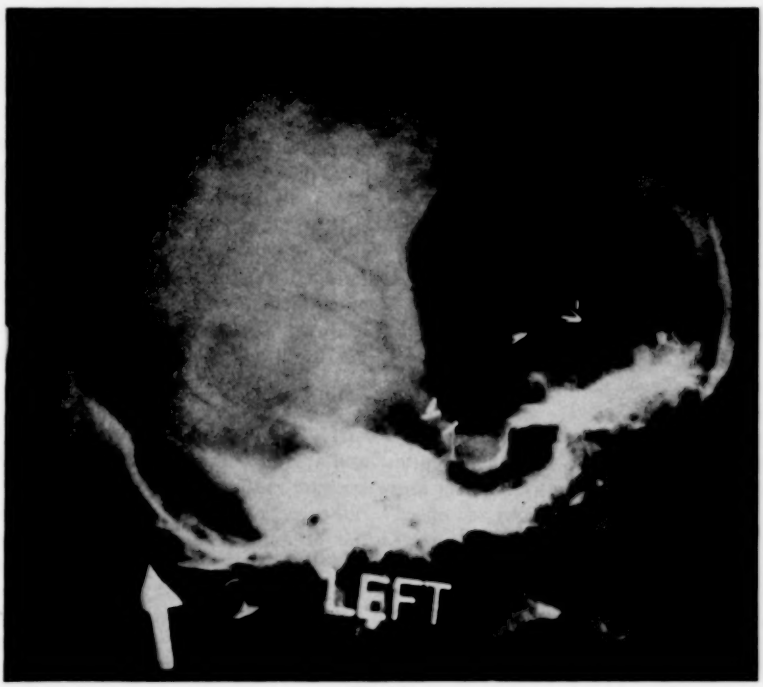


FIG. 1B

FIG. 1. X-rays taken Oct. 26, 1956, show tumor tissue still infiltrating zygoma and sphenoidal wings but completely eradicated from the pituitary fossa area. Compare this with x-ray plate taken May 21, 1954.

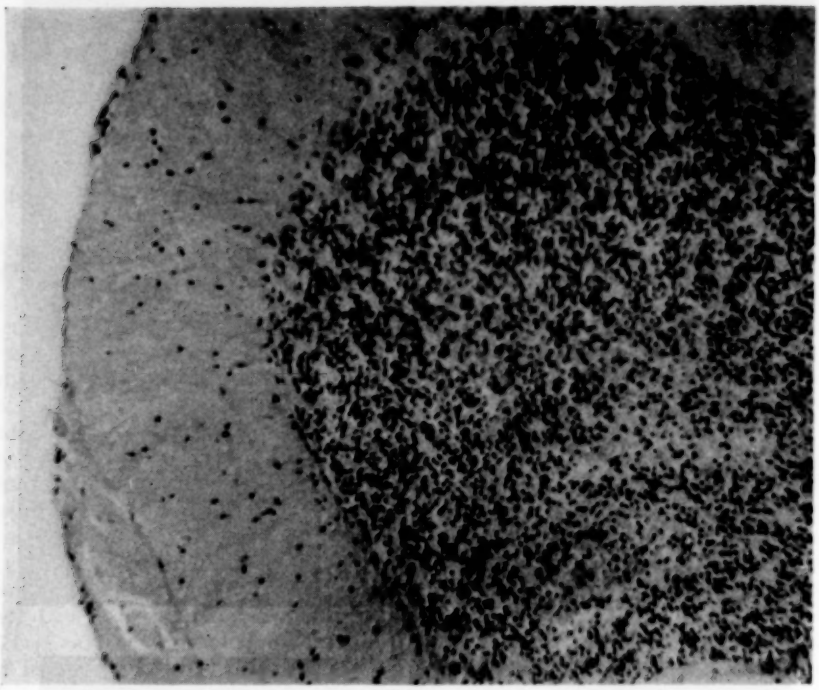


FIG. 2

FIGS. 2–5. Inflammatory reaction in extirpated cerebellar lobe can be plainly seen but there is no sign of metastatic papillary carcinoma.

leptic attack focal in nature which came on after some family trouble. Injections were given once every month.

In April, 1956, the skull x-rays were repeated and showed no extension of the neoplasm.

In Oct., 1956, the skull x-rays showed that there possibly was some extension into the zygoma, but neoplastic tissue in the region of the pituitary fossa seen in the previous plates could not now be seen (fig. 1).

In Oct., 1956, another course of injection was started. The patient has had no epileptic attacks since Nov., 1953, except for the one in Jan., 1955. She shows no signs of raised intracranial pressure. The proptosis of the left eye and partial motor aphasia persist. There has been no behavior upset since 1954. It is now seven years since the last craniotomy for recurrence of the neoplasm.

Case 2: Male, white, age 49 years, confined to bed since craniotomy at a neurological hospital in Oct., 1953. At this time a specimen of neoplasm was removed from the left cerebellar hemisphere. Microscopic diagnosis was metastatic papillary adenocarcinoma.

Hospital report. "On 11/27/53, it was decided to follow patient with x-ray therapy." It is felt that patient, "probably has disseminated metastases and it was considered doubtful x-ray therapy would be of benefit." "On 12/16/53, physiotherapy was started and x-ray therapy was continued."

In Jan., 1955, the patient came under my care. He exhibited double vision, weakness and ataxia of all four limbs, cerebellar type of speech, nystagmus, deafness in the left ear, difficulty in swallowing and a swelling in the left occipital region. He was confined to bed and was helpless as far as ability to feed himself, shave, or care for his toilet wants.

I.M. injections of Bismarsen, Piromen and novocaine were given as outlined above. Injections began Jan. 24, 1955. On Feb. 17, 1955, the patient showed return of motor power in left limbs with diminished ataxia in all limbs

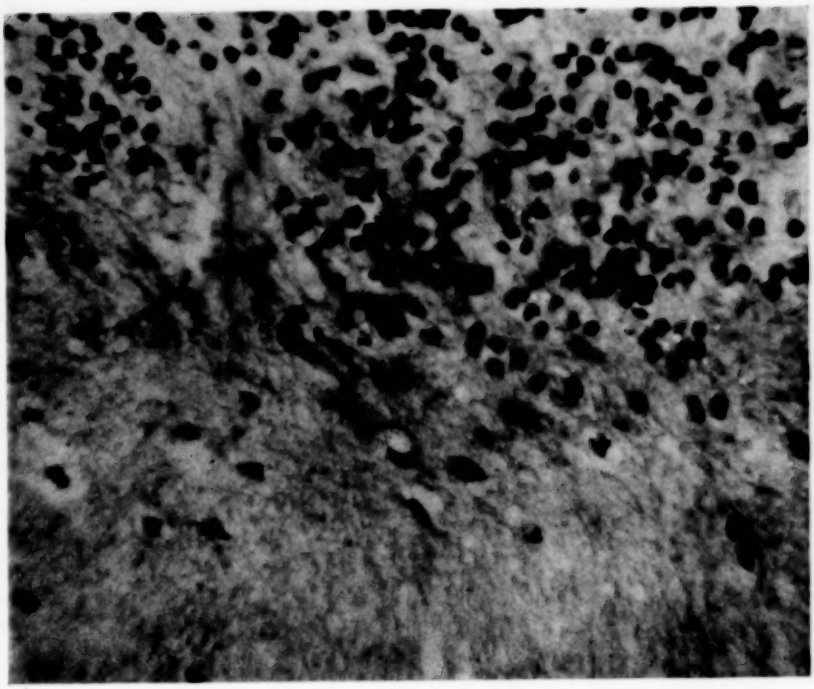


FIG. 3

FIG. 4

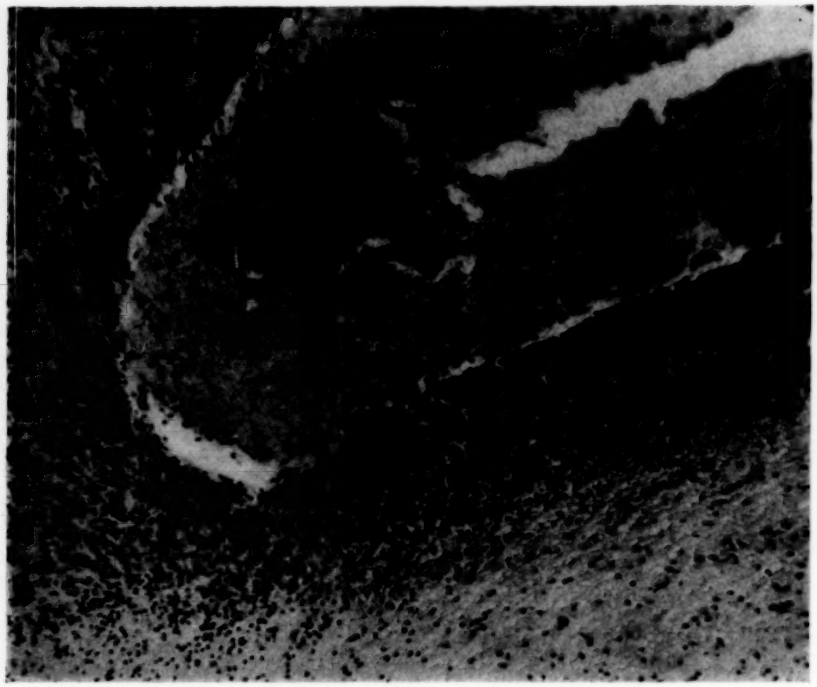


FIG. 5

and was out of bed for the first time. Speech and swallowing were improved. On April 25, 1955, the patient was able to walk with help. Injections were continued twice weekly.

In Oct., 1955, the patient fell and struck the back of his head while trying to get out of bed. Thereafter, his condition deteriorated. He became semistuperous. At this time, it was decided that the involved cerebellar area should be re-operated. Operation was performed and I removed the whole left cerebellar lobe, which appeared completely necrotic (figs. 2–5). Also, a catheter from a Torkildson procedure done at the time of the previous operation was removed. The flow of cerebrospinal fluid was free from the fourth ventricle. The patient responded well after operation. Ate well and spoke with his family. He continued to do fairly well until the fifth post-operative day when he suddenly died with signs of kidney involvement and pulmonary edema.

Microscopic investigation of the cerebellar tissue removed at operation showed no neoplastic cells.

DISCUSSION

While the foregoing method of treatment is presented as being empirical, there is some scientific basis for it.

Gye (5) in 1949 showed that mouse tumors could be propagated. This tended to show that since transference of neoplasms was a fact, we could entertain the possibility that an infective agent may be a factor. McClintock and Friedman (9) in 1945 showed that metals and dyes could be transferred to neoplastic as well as infective tissues by the utilization of the principles of antigen and antibodies.

At the American Association for the Advancement of Science, Gibson Research Conference in 1945, Oakey (10) demonstrated that in 17 cases of malignant disease a specific bacterial polysaccharide had a lethal effect on the neoplasm in each case. This work would also tend to confirm the idea of antigen-antibody effect in neoplastic diseases (6). Also, the work of Gross (4) with leukemic mice makes one feel that even in leukemia an infective agent is at work. McCarty *et al.* (2, 8)

and Gregory (3) have shown with the aid of the electron microscope that there are submicroscopic, spherical bodies which are constantly seen in malignant tissue but are not seen in benign neoplastic tissue.

To my mind, the foregoing work brought forth the following possibilities:

1) That an infective agent, possibly a virus, was a factor in malignant neoplastic disease.

2) That transference of malignancy could take place *in utero* and could be delayed until the embryo reached adult life before showing itself.

3) That there was the possibility of an antigen-antibody effect in neoplastic disease.

4) That certain bacterial polysaccharides had shown a lethal effect on some human malignant neoplasm.

5) That this effect may be due to an antigen-antibody reaction, or at least a hapten reaction (7).

Doyen (1) in 1917 published his findings of the beneficial effect in human malignancies of a neoplastic tissue extract and organic arsenical (Leukolase). Although his work was never accepted, he maintained certain definite cures.

I took the opportunity to try an organic aresenical in combination with a bacterial polysaccharide on two patients suffering from intracranial neoplasm. Since the method was arbitrary as to the number of injections and the time of rest in between courses, there may be some adjustments as to method in the future.

It is my opinion that this treatment has shown the following to be true:

1) The patients did not suffer from mental aberration, epilepsy, or other signs of raised intracranial pressure while getting the injections.

2) Pathological signs showed themselves only when the injections had been stopped.

3) Although the meningioma recurred at first in less than a year and again in 16 months after the first recurrence, it is now more than seven years since the last operation.

4) The meningioma patient has been clinically well since the last course of injections was started.

5) Microscopic examination of tissue removed from case 2 showed no evidence of brain tumor. This may have been due in part to the deep x-ray therapy. However, the doctors in their report state that they did not think that there would be much value in it. Therefore we can assume that destruction of neoplastic cells was due at least in part to the injections of Bismarsen and Piromen.

6) That organic arsenical and bismuth will be "attracted" to neoplastic tissue if combined with a bacterial polysaccharide. In this method, Piromen was used as a "carrying" agent.

7) Comparison of x-rays taken in May, 1954, and Oct., 1956, shows that neoplastic tissue is absent from the pituitary area in the 1956 x-rays but can be plainly seen in this area in the 1954 roentgenograms.

8) The foregoing method is based on sound scientific work and shows evidence of some value. Therefore, it would be worth while to try this "treatment" on a series of cerebral neoplasms which do not respond to more recognized methods of attack.

BIBLIOGRAPHY

1. Doyen, E.: *Surgical Therapeutics and Operative Technique*. New York: Wood and Co., 1917.
2. Gessler, A. E., and Grey, C. E.: Notes on election microscopy of tissue sections. Submicroscopic spherical bodies in carcinoma. *Exper. Med. & Surg., 4:* 307, 1947.
3. Gregory, J.: Election microscopic findings in malignant tissue. *Exper. Med. & Surg., 6:* 390, 1948.
4. Gross, L.: Delayed effects of AK-leukemic cells in mice of the C3H line. *Cancer, 5:* 620–624, 1952.
5. Gye, W. E.: The propagation of mouse tumors by means of dried tissue. *Brit. M. J., 1:* 511, 1949.
6. Golloman, A. L.: Reactions of patients and of tumors to injection of S. marcescens polysaccharide in eight cases of malignant disease. *In* Approaches to tumor chemotherapy. *Publ. Am. A. Advance. Sc.*, 273, 1947.
7. Landsteiner, K.: *The Specificity of Serological Reactions*, Chap. 3. Springfield, Ill.: Charles C Thomas, 1936.
8. McCarty, K., Gessler, A. E., and Grey, C. E.: Notes on the election microscopy of tissue sections. Submicroscopic spherical bodies in human carcinoma 2. *Exper. Med. & Surg., 6:* 368, 1948.
9. McClintock, L. A., and Friedman, M. M.: Utilization of anti-body for the localization of metals and dyes in the tissues. *Am. J. Roentgenol., 54:* 704, 1945.
10. Oakey, R.: Reactions of patients to injection of S. marcescens polysaccharide in nine further cases of malignant disease. *In* Approaches to tumor chemotherapy. *Publ. Am. A. Advance. Sc.* 277, 1947.
11. Rosner, S.: A case of recurrent intracranial meningioma treated by chemotherapy. *J. Nerv. & Ment. Dis., 120:* 287–289, 1954.

1882 Grand Concourse
Medical Arts Building
Bronx 57, New York

THE RESULTS OF CHLORPROMAZINE TREATMENT WITH CHRONIC PSYCHOSES IN DROMOKAITION[1]

P. KOKKORIS,[2] S. KORDAS, P. NIKOLOPOULOS, AND M. YANNIRIS

With the reduction of malaria and venereal diseases and the anticipated control of tuberculosis, mental disorders remain one of the most terrible scourges in Greece as well as in the rest of the world. The problem is more difficult in Greece owing to the scarcity of beds in this field. In a population of 8,000,000 there are 25–30,000 chronic mental patients in need of hospitalization, while only 4,500–5,000 beds are available in all Greece, including those in private clinics. Needless to say, most of our sanitariums are not up to the level of our civilization. In 10 years' time Dromokaition has doubled its bed capacity because of the great demand for admissions.

The usual methods of treatment for acute mental disorders have not been successful with chronic cases to any satisfactory extent. The favorable results with the latter class of cases are not better than those attained spontaneously without any organized therapy. The insistence on treating chronic patients with insulin, cardiazol, electroshock, hypnotherapy, etc., or giving in to the pressure of relatives to continue the treatment only impressed us that we were getting nowhere. Because of the inadequacy of our therapeutic methods the patients entering sanitariums exceed those who are discharged as cured, and this difference is continuously increasing although the facilities for caring for them remain static.

Psychosurgery which for a time appeared to contribute to the solution of this major problem of chronic psychotics only partially justified the hopes placed on it. The mortality rate, the complications, the resulting change in the personality, the uncertainty of the results of treatment, the relapses and the limited indications were the most important reasons obliging psychiatrists to search for other better and less dangerous methods of therapy. This was the situation when chlorpromazine appeared on the therapeutic horizon.

The first production of the drug was made by the factory Specia in Paris as #4560 and was introduced on the market as Largactil (Europe) and Thorazine (America). This drug, which has a special antihistaminic action, belongs to the amines and is derived from phenothiazine. According to Laborit, chlorpromazine proved to be a valuable drug in surgery since it produces a type of hibernal numbness; a prevention of diffusion of a stimulus through the body and simultaneously a reduction in the function of glands, thus reducing surgical shock and post-operative complications.

The introduction of chlorpromazine to psychiatry was made three years ago when several French workers treated mental patients with combinations of chlorpromazine pentothal, phenergan, diparcol, phenobarbital, soneryl and amytal in a complicated procedure. The results of this hypnotherapy were not particularly encouraging and not quite free of dangers.

The communications of Delay and Deniker, in the Congress of French Neurologists and Psychiatrists held in Luxemburg in July, 1952, mark the beginning of the treatment of mental disease with chlorpromazine alone. Since then reports on the subject are increasing throughout the world without any final consensus as to the dosage, the way of action, or the effectiveness of its application. We have applied the method as the exclusive treatment in B Clinic of Dromokaition since the first of July, 1955.

The present study deals with our observations and results of a follow-up of 194 patients who were treated exclusively with chlorpromazine since July 13, 1955. Of these patients 170 were classified as schizophrenics, 6 as manic depressives, 5 as epileptics and 13 in other categories of mental illness (see table 1). All of these patients were treated previously in Dromokaition or elsewhere with

[1] Read before the Medical Society of Athens, Greece, February 11, 1956, and the Neurological and Psychiatric Society of Athens, February 14, 1956.

[2] Director of the B Clinic of Dromokaition Mental Hospital, Athens, Greece.

various intensive and prolonged treatments with electroshock, metrazol, insulin, hypnotherapy, fever therapy and by repeated combinations of these. Twenty-three of the patients had undergone a bilateral prefrontal lobotomy (Freeman and Watts).

The greater number of our patients represented unsolved medical and administrative problems owing to their chronicity and their aggressive, confused and excited states. No environmental influences or any psychotherapeutic applications were possible in treatment as these patients were out of contact. They remained in the same wards and beds as previous to chlorpromazine therapy, and all other treatments were discontinued including hypnotics and sedatives. There was no special handling of patients under therapy. In a very few patients we combined the treatment with electroshock and reserpine, but the results were no better than with chlorpromazine alone; therefore any combined treatment was discontinued.

For cooperative patients the initial dose was 25 mg. three times daily for the first month, after which 50 mg. t.i.d. were given. For uncooperative patients treatment was started with intramuscular injections of 25 mg. t.i.d. at 7-hour intervals, thus securing sleep. Under the influence of the injections the patients became quiet, thus enabling us to replace the injections with oral therapy. Oral administration was preferable because of the local aseptic inflammatory reaction from injections of high dosage and the greater expense involved as compared with tablets.

Usually the patients accepted the tablets four to five days after the beginning of the treatment with injections. Only one of the patients refused to cooperate, obliging us to discontinue the treatment. Special attention was necessary for some patients because of their attempts to disobey the nursing personnel and avoid taking the drug by hiding it under the tongue or by self-induced vomiting. The quantity of the drug was increased every third day by 25 mg. to bring each patient to the appropriate dose.

At this point we wish to stress that the action of chlorpromazine affects more than a few symptoms of the disorder, a fact that is accepted by most researchers on the drug, and that the results of chlorpromazine therapy

TABLE 1

	Single Admission		Multiples Admission	
	Continuous			
	0–5 years	Over 10 years	0–10 years	Over 10 years
Schizophrenia				
Simple	5	5		
Hebephrenic	30	47	5	1
Catatonic	3	8	2	
Paranoic	39	13	12	
Manic-depressive psychoses	1	1	3	1
Miscellaneous				
Epileptic psychoses		4		
Psychopathic personalities	1		1	
Perverse and retarded	5	2		
Alcoholic psychoses				
Psychoneuroses		1		
Senile psychoses	1			
Progressive general paresis		1		
Total	85	82	23	2

are much better than those of other empirical methods such as insulin and electroshock. We reached these conclusions from the results with chronic patients who were treated previously with those methods without any benefit. Most important is the fact that chlorpromazine is not as dangerous as the other methods mentioned above.

From the follow-up of patients for many months we concluded that chlorpromazine treatment of psychotics is a new empirical method of treatment. The action is more than on isolated symptoms and is in many points analogous to treatment with insulin. As with insulin small doses causing slumber or subcoma (subcoma insulinotherapy) are sufficient to improve or cure acute psychoneuroses and psychoses, so with chlorpromazine, small doses (200–250 mg.) which cause slumber and a subjective feeling of languor are sufficient to cause spectacular improvements on psychotics and neurotics.

In order to get a favorable therapeutic result on chronic psychotics with insulin we continuously increase the dose until we produce a deep, smooth and long-lasting coma, which must last in time and depth and be repeated many times. Similarly with chlorpromazine the dose must be increased continuously until the body is saturated with it. Frequently,

we obtained a therapeutic result only when large doses were given and the patient showed clear signs of a deep saturation with the drug, which was apparent from an intense sleepiness, Parkinsonism and inability to sit. The axiom of Boss seems valid for chlorpromazine also; he said of all the empirical shock treatments: "The nearer to death the better the result."

The doses were reduced gradually in our patients after their saturation with the drug and were continued for a long time in conservative doses, which fluctuated between a half and a third of the dose. That there are methods of treatment with small or large doses of chlorpromazine, supported by many authors, is not valid according to our view. However, in our experience we must find for every patient the proper dose which will have therapeutic results, as is the case with insulin-therapy. Let us not forget that in psychiatry we deal not with diseases but with patients. Consequently, the daily dose of chlorpromazine fluctuated in our patients from 150 mg.–975 mg. (table 8).

In this study most of our patients took the drug continuously in doses which are given in the table 8 for more than 7 months, and the treatment is still continued. We have not included in this report patients receiving less than a month's treatment.

The follow-up of the patients under treatment was made by the nursing supervisors of the wards, the physician members of the Clinic staff and by the first of the authors of this study, who as the Director of the Clinic tried to have 10 to 15-minute interviews with each one of the patients at least once or twice weekly. The follow-up extended beyond the wards to the athletic grounds, to the job areas, to various social functions of the hospital (parties, etc.) and to other such functions of occupational therapy.

The therapeutic results reported, as in tables 3 and 4, consist of the combined judgment of the members of this communication and the nurse supervisors of the wards. Each one of the above-mentioned evaluated the patients separately under treatment after a long lasting follow-up and observation. For the evaluation of the therapeutic result we had in mind the patient's condition on the day on which treatment was begun. We defined this condition conventionally with zero (0). The therapeutic result was considered "excellent" and was graded 9 or 10 when all the psychotic symptoms yielded, the patient was discharged from the hospital, adapted himself absolutely to the social and familial environment and worked in his previous job or a similar job satisfactorily. The result was characterized "good" when under the influence of treatment the patient was discharged from the hospital free of symptoms, adapted himself well to the social and familial environment and worked either in his previous job unsatisfactorily or worked in another job requiring a less mental effort. This result was graded 8. "Average" was the classification given the result when the patient improved to such a degree that he was discharged from the hospital, adapted more or less well to the familial environment, but was unable to work, or worked in a job much inferior to his previous work, and unsatisfactorily. This was graded 5 or 6. The results were characterized as slight improvement when the patients improved to such a degree as to no longer constitute a problem for the hospital, when he worked in simple jobs in the hospital, but was unable to be discharged and live with his family. This was graded 3 or 4. When no improvement at all or a valueless one was noted, the result was characterized as stagnant, and graded 2, 1, or 0. Let us stress that during the 7 months in which our patients were treated with great doses of chlorpromazine, we observed not one aggravation of mental symptoms, no deaths occurred and at no time were the lives of the patients endangered by the drug.

In deducing results we considered patients' hallucinations, illusions, paranoid ideas, excitement states, aggressiveness, soiling themselves and their surroundings, behavior toward other patients and personnel, ability to establish social and friendly relations with other patients and personnel and adaptation to the social environment. The condition of the other chronic patients who remained in the same wards and who were not treated with chlorpromazine or other treatments was used as a measure of comparison and control of the results.

Another measure of comparison was a group consisting of 15 patients treated with

TABLE 2.—MANIC-DEPRESSIVE PSYCHOSES

Results	Single Admission						Multiple Admissions		
	0–5 years			Over 5 years			All over 5 years		
	Duration of treatment in months			Duration of treatment in months			Duration of treatment in months		
	1–2	2–4	4–7	1–2	2–4	4–7	1–2	2–4	4–7
Excellent									
Good									2
Average									
Small improvement						2		1	
Same condition				1					
Total				1		2		1	2

TABLE 3.—SCHIZOPHRENIA

	Duration of Treatment in Months			Results				
	1–2	2–4	4–7	Bright	Good	Average	Small improvement	Same condition
Simple	3	2	5			1	4	5
Hebephrenic	7	7	69		2	6	63	12
Catatonic		1	12			1	11	1
Paranoic	3	10	51	4	13	15	29	3
Total	13	20	137	4	15	23	107	21

TABLE 4.—MISCELLANEOUS

Diseases	Duration of Treatment in Months			Results				
	1–2	2–4	4–7	Bright	Good	Average	Small improvement	Same condition
Epileptic psychoses			5					5
Senile psychoses		1					1	
Alcoholic psychoses								
Psychopathic personalities		1	2				3	
Perverse and retarded			8			3	2	3
Progressive general paresis			1				1	
Psychoneuroses			1				1	
Total		2	17			3	8	8

great doses of Serpasil who were observed and followed the same way as the patients treated with chlorpromazine. Let us stress again for the exact appreciation of chlorpromazine treatment results that our patients were chronic psychotics treated without previous success with all the known empirical methods, and also with bilateral prefrontal lobotomy (23 cases). Most of them should have been considered incurable.

RESULTS

As indicated in the tables (2, 3, 4, 6) 170 schizophrenics underwent treatment as follows:

Simple schizophrenia	10
Hebephrenic schizophrenia	83
Paranoic schizophrenia	64
Catatonic schizophrenia	15

Eighty-two patients of the group had been treated in the hospital for more than 5 years.

In this category we obtained the following results:

Excellent	1 (1.2%)
Good	8 (9.4%)
Average	6 (7%)
Small improvement	48 (59.2%)
Stagnant	19 (23.2%)

In the following 87 cases of schizophrenia treated in the hospital less than 5 years, the results were as follows:

Excellent	3 (3.47%)
Good	9 (10.32%)
Average	18 (20.70%)
Small improvement	52 (59.75%)
Stagnant	5 (5.76%)

As is indicated in the relative tables, best results were observed in the paranoic schizophrenia, followed by the hebephrenic, catatonic and simple schizophrenia.

The time of the duration of the illness is considered to be only the time of their admission to Dromokaition although this time does not represent completely the duration of the illness from its early beginnings. We considered this principle the better one because it is difficult and sometimes impossible to define exactly the time of the onset of the illness and the time of the patient's wandering outside the hospital from doctor to doctor.

The results of chlorpromazine treatment on 23 patients who had undergone bilateral lobotomy, all schizophrenics but one obsessive-compulsive psychoneurotic, are as follows:

Excellent	1 (4.4%)
Good	1 (4.4%)
Average	3 (13.2%)
Small improvement	13 (56.5%)
Stagnant	6 (26%)

These results reinforce the opinion of one of us (P.K.), who in a monograph related to lobotomy now being printed, supports the views that irrespective of the injury it causes, lobotomy does not necessarily constitute the terminus of therapeutic attempts, and that further therapeutic attempts are practicable. Our study included 6 diagnoses of manic depressive psychoses. The results of treatment, as noted in the appropriated table, are better than in schizophrenia. We stress that on patients suffering from manic-depressive manifestations during their whole life, with more than 37 admissions to the hospital and more than 30 years hospitalization, the differential signs of the disease remain intact.

Chlorpromazine was also applied on various organic diseases, epilepsy, mental defectiveness alcoholic psychoses, drug addiction, general paresis, etc., with results varying from bright to worthless. Surprising results were obtained on a chronic general paretic and on a mental defective, who were unsolved clinic problems because of their continuous excitement, their screams, nakedness and their continuous miserable condition from the point of view of dirtying themselves and the wards. Both of them quieted completely, they eat in the dining room of the ward, do not tear their clothing, go to the W. C. alone, do not scream, and although our contact with them is impossible, they have ceased to be considered clinic problems. Our impression is that on chronic organic psychoses such as senile dementia, chronic general paresis, mental defectiveness, chlorpromazine exercises a greater sedative action when given in small doses (150–225 mg.). This does not apply to the epileptic psychoses on which, at least in our cases, no serious results obtained. Chlorpromazine given in high doses exercised no action on epileptic crises, nor did we observe any result from the combined action of chlorpromazine given simultaneously with barbiturates or hydantoine's salts.

As it is noted in the previous tables a great number of our patients treated with chlorpromazine showed a "small improvement" which, however, changed the appearance of our wards. Thus now we have no isolation of patients (the restraint jackets have not been used in Dromokaition for many years). The patients appear properly clothed, their nutrition has improved, the damages on the establishments and on the hospital equipment are restricted to the minimum, cleanliness is excellent, and for the personnel service in the so-called "disturbed" wards does not consist now of heroism.

The appropriate table on the changes achieved in the wards of "disturbed" patients speaks for itself (table 5). It is to be noted that chronologically the beginning of improvement was not the same for all patients. Many of them improved essentially from the first month of treatment although in others the

TABLE 5.—Disturbed Men and Women

	Total Number		Dirty		Naked		Agressive		Especially Dangerous		To Occupational Therapy	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
July, 1955	31	20	15	10	6	6	16	11	2	5	2	2
November, 1955	30	19	6	6	3	3	3	5		2	4	6
February, 1956	29	19	5	6	2	2	3	3	2	2	5	6

TABLE 6.—Patients Who Have Been Previously Lobotomized

Results	Schizophrenia	Manic-Depressive Psychoses	Miscellaneous
Excellent	1		
Good	1		
Average	3		
Small improvement	11		2
Same condition	5		
Total	21		2

first signs of improvement were observed only after 3–4 or more months of continuous therapy. In all the patients, however, who showed improvement, this improvement was more apparent after the continuation of treatment and the increase of the dose. The improvement is maintained as the drug is administered continuously. When, against our will, we were obliged to discontinue the drug for most of our patients for 3–4 days, we saw the previous clinical state appear again. The patients again showed the same improvement a few days after the drug was administered again.

This is the weak point of the method, that the treatment of chronic schizophrenic psychoses and organic psychoses must be continuous for an indefinite time. Our experience is chronologically restricted for the manic-depressive psychoses, and we cannot support the same view for these diseases. It is probably that the drug should be given only during the crises and not continued in the intervals. In our manic-depressive cases we had no intervals of the diseases so the administration of the drug was continuous. In our opinion the drug must be given continuously for a long time after the patient is discharged from the hospital in the same manner as is done with epileptics even after the elimination of the epileptic crises.

We have the opinion that chronic psychotics who have improved with chlorpromazine continue to need it as patients suffering from diabetes need insulin. We know, however, patients of our clinic who after their discharge from the hospital did not continue the drug, although we advised it, but retained, however, their acquired improvement.

We did not notice addiction to chlorpromazine although we gave it to drug-addicted patients. Nor did we observe any pathological signs after the discontinuation of the drug, apart from the reappearance of the mental symptoms as is stressed above.

Complications and Side Effects

The complications and side effects caused by the drug were studied as completely as possible. The result of this attempt is recorded in table 7. One of the more common complications was hypotension which fluctuated between 1 and 5 degrees but which, however, never reached dangerous levels. There were no symptoms of acute arterial hypotension or collapse or myocarditis in contrast to the findings of other workers. Incidentally, one of us noticed a patient treated with chlorpromazine outside of the hospital who had a pronounced tachycardia (pulse rate 140 per minute). Also a similar complication was noticed in chlorpromazine treated patients of another clinic. The percentage of patients with hypotension amounted to 50.2%. In not one of the cases, however, did we decrease the dose or discontinue the drug owing to hypotension.

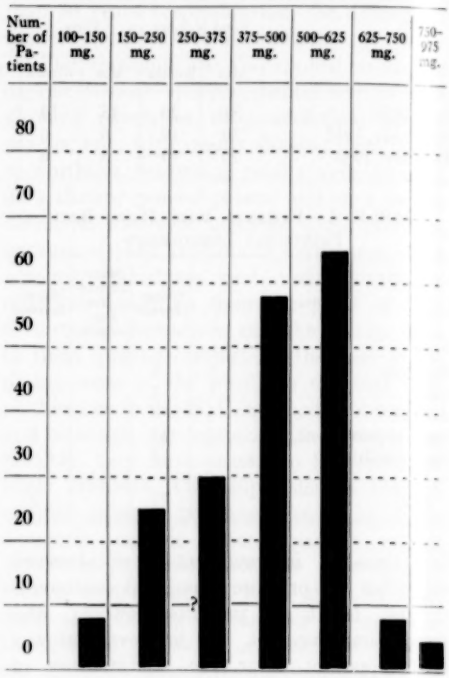
The most serious and usual complication in our statistics was Parkinsonism (fig. 1). As was indicated in the table, 65% of the cases showed this reaction.

The frequency and importance of Parkinsonism will be fully appreciated if we keep in mind that these numbers include only patients with a complete and clear symptomatology

TABLE 7

Complications and Side Effects	Number of Cases	Per Cent	Total Per Cent
1. Hypotension			
a. From 0–1 cc.	32	18	
b. From 1–2 cc.	29	16	
c. From 2–3 cc.	19	10.6	50.2
d. From 3–4 cc.	7	4.5	
e. From 4–6 cc.	1	0.6	
2. Somnability			
a. Mild	6	3.5	30.5
b. Severe	45	27	
3. Skin lesions			
a. Simple dermatitis	5	2.5	
b. Desquamating dermatitis	45	27	32
c. Ulcerative dermatitis	5	2.5	
4. Parkinsonism			
a. Mild	53	29	
b. Clear	8	5	
c. Intense	51	28.2	74.5
d. Inability to sit still	25	12.3	
5. Epilepsy			
a. Typical (epileptics)	5	2.8	
b. Typical (for the first time)	1	0.8	3.6
6. Edema	4	2.3	2.3
7. Jaundice	4	2.3	2.3
8. Headaches	12	6.9	6.9
9. Diarrhea	3	2.3	2.3
10. Constipation	35	19.6	19.6
11. Hematological disturbances	4	2.1	2.1

TABLE 8.—CHLORPROMAZINE DOSAGE



of Parkinsonism (masked facial expression, drooling, extrapyramidal stiffness, Parkinsonian tremor, characteristic gait and speech). Patients manifesting a slight immobility of the face, poverty of automatic movements and a slight Parkinsonian gait were not included in the above figures. If these were included, the complications of Parkinsonism would be present in all cases under treatment. The first symptoms of Parkinsonism usually appear with the dose 250–300 mg., and the whole classical manifestation of the disorder appears with 400–600 mg. Sometimes, however, we obtained a complete manifestation with a much lower dosage such as 150–200 mg.

Manifestations of toxic Parkinsonism thus created are surprisingly analogous to post-encephalitic Parkinsonism. No confusion is possible between this toxic reaction and the pseudo-Parkinsonism or the drug catatonia (Bulbocapnine) as some workers claim (Baruk, etc.). Neither did we observe any connection between this Parkinsonism and that resulting from other drugs, especially barbiturates

FIG. 1

since our patients did not receive any drug but chlorpromazine. Parkinsonism consequently is the most usual and expected complication of chlorpromazine treatment. Thus the opinion of those workers who ascribe the selective action of this drug on the basal ganglia and the structures of the diencephalon and mesencephalon and the neighboring reticular tissue is justified. This complication was so pronounced as to oblige us to completely discontinue the drug in a number of patients and in others to reduce considerably the usual dose.

In 20 patients we continued the treatment at the same dose level giving simultaneously anti-Parkinsonism drugs (Diparcol, but mainly Artane in doses of 6–10 mg.). The drug-Parkinsonism disappeared within 6–8 days after the discontinuation of the drug although it existed following a gradual lessening of the dose for 10–15 days. With anti-Parkinsonism treatment (Artane) the manifestations improved essentially within 3–5 days.

Noted in the relative table as a special complication is inability to sit still. Although it is a characteristic symptom of the Parkinsonian syndrome, we stress it especially because its intensity was sometimes so great and its frequency so unusual. We stress it further because nowhere in the bibliography accessible to us did we find reference to this symptom. In the beginning it appeared strange to us to hear patients complaining that they were unable to sit down, to lie on their beds, or to remain standing on the same spot. They were obliged to walk continuously or to transfer their body's weight from one leg to the other. Their existence was very annoying to them and to the other patients of the same ward because they were obliged to get up frequently and walk, to go to bed, thereafter, to get up again, etc. This symptom yielded immediately to the administration of 6–10 mg. Artane, and it was possible in this way to continue the treatment.

Slumber and lethargy were also among the more frequent manifestations of side effects. These appeared with doses of 200–250 mg. daily, but they accompanied regularly much greater doses. As a matter of fact, chlorpromazine slumber in all its gradations varied essentially from the sleep caused by barbiturates mainly because the patients would be awakened easily and were able to do calculations, to obey directions, and take care of their physical needs. We gained the impression that slumber lasted only during the 4–6 weeks from the beginning of the treatment and that with the continuation of treatment, and even with increased doses, gradually subsided until it disappeared. Not infrequently there were cases where the initial slumber was followed by a worrying insomnia.

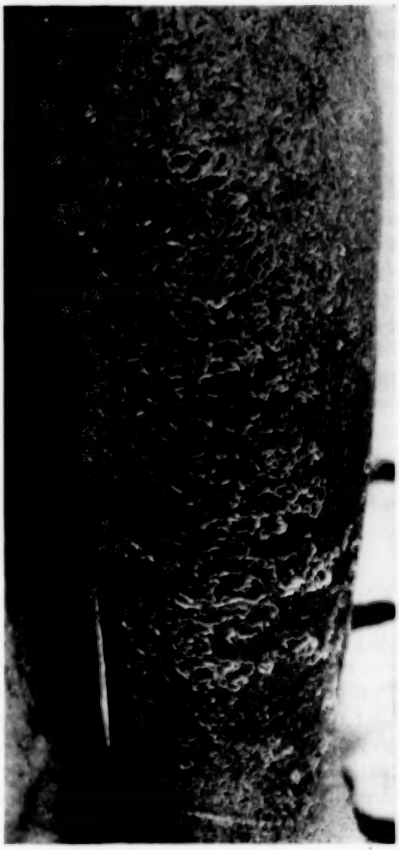


FIG. 2

Skin manifestations were one of the commonest complications. Almost all the patients showed a darkening of the facial skin and of those parts of the skin exposed to sunlight. Conjunctiva were inflamed in the areas between the eyelids open to sunlight. Skin manifestations appeared in 32% of the patients and took the following forms: simple dermatitis 2.5%; peeling dermatitis (fig. 2), 27%; ulcerative dermatitis (fig. 3), 2.5%; and swelling, 2.3%. In some cases owing to the great in-

FIG. 3

tensity and extension of skin manifestations, it was necessary to discontinue the treatment.

In other cases the skin manifestations were similar to the clinical picture of pellagra and scurvy. The administration of vitamins B and C with the simultaneous administration of chlorpromazine did not exercise any influence on the skin manifestations. Only the discontinuation of chlorpromazine achieved the elimination of skin manifestations within 8–10 days. We gained the impression that sunlight made the skin more sensitive in some cases to chlorpromazine. The simultaneous administration of antihistaminic drugs for a short time and the lessening of the chlorpromazine doses did not succeed in eliminating skin manifestations.

Jaundice was a rather infrequent complication in our patients, appearing in 2.3%. There was only a slight coloring of the conjunctiva so that the treatment was not altered.

Systematic blood examinations permitted us to follow our patients closely. However, no changes in blood (non-granular leukocytes, leukopenia, etc.) required any discontinuation or lessening of chlorpromazine dosage.

A regular control of sedimentation rate showed a slight increase (2.1%).

In the gastrointestinal system there were intense diarrhea and pains in the epigastrium during the period of administration of high doses of chlorpromazine. These symptoms yielded as soon as the drug was discontinued or reduced. The most frequent and insistent annoyance associated with the digestive system, however, was the intense constipation which tortured a number of patients under treatment. This constipation did not yield with a controlled diet and with mild laxatives. In these cases, we were obliged to discontinue the treatment or to continue it with a simultaneous administration of laxatives.

Another complication noticed in a very few cases was the swelling of masculine breasts. Owing, however, to the lack of control from the beginning of treatment we observed this complication with reservation although our patients assured us that they noted the increase of their breasts during the treatment. A comparative examination of patients under treatment with those not under treatment showed an enlargement of breasts to a greater degree for those under treatment.

SUMMARY AND CONCLUSIONS

One hundred and ninety-three chronic patients of Dromakaition B Clinic were studied under chlorpromazine treatment for seven months. These patients are continuing under

treatment. Forty-three of these patients clearly improved and have been either discharged from the hospital or are about to be discharged. One hundred and four other patients showed a satisfactory improvement but are not able at the present time to leave the hospital.

It is indicated from the results that chlorpromazine constitutes an important progress in the treatment of mental diseases. It achieves better treatment results in comparison with the other classic empirical methods, at least in chronic psychoses, considering especially its safety.

There are no arbitrary small or large doses; each patient requires chlorpromazine dosage to be individually adapted to him. The toxicity of the drug is rather small.

Since our experience is very limited, we cannot say when we may discontinue the treatment. Our view is that chlorpromazine must be administered for a long time after the patient's discharge from the hospital, probably under a conservative dose for more than a year. That is to say, we must do the same as in epilepsy where the treatment continues two years after the elimination of seizures.

The cost of treatment, with the current prices, for a patient given average doses (500 mg.) daily is about 400 drachmae per month. If these are the expenses required for a patient to be discharged from the hospital and returned to contact with his social and familial environment, they seem to be a small cost for a great service offered to the individuals and society as well.

In conclusion, we would like to thank warmly the Administrative Council of Dromokaition Hospital for its financial assistance in the completion of this work, and also the drug firms Cooper (Athens) and Specia (Paris) for their prompt and generous help which rendered possible the continuation of treatment of indigent patients of the hospital and therefore achieved a degree of improvement impressive in the light of restricting realities in Greece.

76 Solonos Street
Athens, Greece

BIBLIOGRAPHY

Laborit (H. et G.) *Excitabilité neuro-musculaire et équilibre ionique. Intérêt pratique en chirurgie et en hiernotherapie.* Masson et Cie, Paris 1955.

Freeman and Watts. *Psychosurgery.* 2nd edition. Thomas. Springfield, Ill. 1950.

H. Baruk, J. Launay et J. Berges. La thérapeutique par la chlorpromazine. Physiologie expérimentale. Physiologie clinique. *Ann. Méd. Psychologiques, 1:* 705–772, 1955.

PSYCHOTHERAPEUTIC ALTERATION OF A PHYSIOLOGIC STRESS RESPONSE

SANFORD I. COHEN, CAPTAIN, USAF (MC),[1] ALBERT J. SILVERMAN, CAPTAIN, USAF (MC), GEORGE ZUIDEMA, CAPTAIN, USAF (MC), AND CECILE LAZAR, B.S., M.A.

INTRODUCTION

In previous papers, the authors presented preliminary evidence relating the affect state of subjects to their cardiovascular stress responsivity on the human centrifuge (2, 7, 8). It was speculated that emotional factors are significant in the inter and intra individual variations in tolerance to gravitational forces. Early results suggested that the emotional influences on black-out levels were dependent upon blood pressure variations, produced by various affective states, and that these influences were in part mediated by the secretion of adrenaline and nor-adrenaline. Focused interview techniques aimed at evaluating the degree of anxiety and aggressive impulses successfully predicted the level of G-tolerance of various subjects (2). It was felt that anxiety might be associated with the excessive release of adrenaline and peripheral vasodilation while aggressive, controlling or hostile impulses were associated with nor-adrenaline increase and peripheral vasoconstriction. A subject's ability to withstand high levels of G-stress is dependent on the capacity of his cardiovascular system to compensate for the hydrostatic forces pulling blood away from his head and eyes. Black-out occurs when insufficient blood reaches his retina. Compensatory reflexes cause a peripheral vasoconstriction and lessen blood pooling in the lower extremities. Since nor-adrenaline is thought to be released at the sympathetic neural endings and is a peripheral vasoconstrictor, high nor-adrenaline levels would be expected to allow for higher G-tolerances (3). Goodall and Meehan have demonstrated that high nor-adrenaline levels are, in general, associated with higher G-tolerance (4).

The preliminary findings were further confirmed when adrenaline-nor-adrenaline levels, affect state and the G-tolerance of a series of subjects were evaluated (8). High tolerance to centrifugal stress was associated with high nor-adrenaline levels and low tolerance with low nor-adrenaline and frequently with high adrenaline levels. The low G-subjects had high levels of anxiety while the high G-subjects had low levels of anxiety and a high degree of aggressive expression. The relationship of blood pressure changes to small doses of mecholyl (5 mg.) and affect state was described (8). Angry, hostile feelings or an aggressive controlling, non-anxious demeanor was associated with blood pressure increases, high levels of urinary nor-adrenaline and low levels of adrenaline. Contrarily, persistent blood pressure decreases followed mecholyl injection when the subject was overtly anxious, and this was associated with high levels of adrenaline and low levels of nor-adrenaline.

It should be pointed out that these variations do not refer only to interindividual differences. Day-to-day intraindividual variations also appeared related to affect state and catechol amine changes.

Further confirmation of the relationship of specific affective factors to G-tolerance was obtained by the successful differentiation of subjects who had high and low average G-tolerance by a projective test developed at this laboratory (7). This test was designed to elicit maximal information about the subjects handling of aggressive impulses. Although other personality factors could be interpreted from the test protocol, the evaluation of the subjects responses was focused mainly in judging aggressive factors and anxiety proneness.

If the above hypothesis is valid, then it should be possible to alter subjects G-tolerance by producing changes in affect state. This paper describes a unique opportunity which permitted the clinical testing of the concepts. A student pilot was referred to this

[1] From Stress and Fatigue and Acceleration Sections, Aero Medical Laboratory, Wright Air Development Center, Wright-Patterson Air Force Base, Ohio.

laboratory for evaluation of his G-tolerance. During the course of his examination incidents occurred which allowed the authors to utilize the theoretic framework which had been postulated as a basis for using psychotherapeutic measures to deal with an apparent failure in the subject's compensatory mechanisms to G-stress.

Summary of History

The patient was a 21-year-old student "jet" pilot who was referred to this laboratory for evaluation of his G-tolerance. He had several episodes of black-out and unconsciousness in jet trainers when his instructor was flying the aircraft. He was initially referred to another center where a medical, neurologic and neuropsychiatric workup was done. The workup was negative, and no basis for his black-out episodes was found. He was sent to this laboratory to establish his tolerance to centrifugal stress on the human centrifuge. Further, he was to be evaluated by the psychophysiologic battery developed here which was focused primarily in judging the psychologic, biochemical and physiologic areas considered to be related to G-tolerance. This workup was in no way intended to represent a complete physiologic and psychologic survey.

Psychophysiologic Test Battery and Results

The testing schedule consisted of the following procedures:

1. Centrifuge acceleration studies in which the subject's black-out level is established; he is tested on at least three separate days. During the time of centrifugation, cardiovascular and bioelectric (skin resistance) measures are done. Urines are collected on one test day, before and after the runs, for bio-assay of adrenaline and non-adrenaline.

2. Psychologic testing: The patient is given several tests prior to being centrifuged. These included: a) The Aero Medical Focused Thematic Test: This test has proved rather successful in differentiating average high G and average low G-subjects (7). b) Draw yourself in a plane test: This is directed at evaluating the patients concept of himself in relation to a plane. It is aimed at detecting some of the symbolic meaning of the plane, particularly in terms of the degree of incorporation into the body image or self-concept of the pilot. In addition, it was hoped that information regarding the type of impulses which were displaced to flying and/or the aircraft would be elicited (6). c) Standard psychologic tests: Rosenzweig picture frustration test, modified Taylor scale of manifest anxiety, Freeman anxiety scale, Shipley Hartford, and the Rorschach test were administered. d) Aero Medical Socio-cultural questionnaire: This questionnaire was designed to elicit information regarding sociocultural attitudes and the manner in which aggressive drives are handled (6).

3. Biochemical testing: a) Waking adrenaline and nor-adrenaline levels are obtained on control days to establish the average level of hormones released. These assays are also done before and after centrifuge stress to assess the catechol amine response to G-stress. b) Urinary hippuric acid determinations: These were carried out as measures of the degree of chronic free floating anxiety (1).

4. Psychiatric interviews: These are aimed primarily at evaluating the anxiety proneness and the manner in which the patient deals with aggressive impulses. The meaning of flying to the patient is also investigated. A detailed anamnesis of the black-out incident and events related to it in time is done during the interview.

Hence an attempt is made to examine the psychophysiologic structure of the patient in a specific area which has been found to be related to G-tolerance variations. Information is then sought to determine if events had occurred which provoked affective reactions which would be responsible for neurohormonal and physiological alterations leading to a change in G-tolerance.

The patient's Focused Thematic Test protocol revealed that he told stories in which aggressive incidents were readily portrayed and in which he usually identified with the aggressor. The stories were active with the hero usually being independent and persisting in goal directed behavior. These factors are those identified in persons with high G-tolerances. The Rosenzweig test revealed a predominance of extrapunitive hostile re-

sponses. The Taylor scale and Freeman test showed low manifest anxiety, and this correlated with his hippuric acid excretion level which was considered low. (The patient's level was 1.4 grams excreted in 1 hour after i.v. injection of 1.77 gram of sodium benzoate. Low G-subjects usually have excretions over 2 grams). Other psychologic tests revealed that the patient was able to express aggression easily although often using displacement and substitution.

The psychiatric interviews, in general, agreed with the test findings. Although his level of overt anxiety was low, it became apparent that one of the subject's major areas of emotional vulnerability was fear of male authority figures and his inability to express aggressive feelings towards them. He handled this by the avoidance of situations in which he might be attacked or controlled by these authority figures. When he could not avoid conflict with them, he found it necessary to control his aggressive feelings and submit without an active struggle. In this kind of a situation he seemed prone to anxious feelings.

The patient's initial centrifuge runs indicated that the psychologic tests had correctly identified his G-tolerance. His black-out determined on the first day of centrifuge testing was 4 G (high). The findings indicated that his cardiovascular reflexes were capable of maintaining compensatory activity for high levels of gravitational stress.

On the afternoon of the fourth day of testing, the subject was taken to the centrifuge for his second run. On his first ride at a very low G, the patient lost his peripheral vision (first sign of impending black-out). On his third ride which was to have reached 3.5 G, the subject blacked-out before the peak of acceleration was attained. The centrifuge was stopped, and he was examined by the physician on duty. Clinically, the patient appeared in a near panic state, he was sweating, had a hand tremor and was pale. He stated at that time that soon after the centrifuge began he could not see. He realized he should do something, but he could not get his hands to move.

Since it had already been established that this patient was capable of withstanding high G levels, the physician in charge felt the incident was related to a change in tolerance level due to emotional factors. He was then seen in a psychiatric interview aimed at exploring the cause, type and intensity of his anxiety. It was planned then to make attempts to ameliorate the apprehension.

Summary of Interview and Post-interview Testing

The patient appeared apprehensive when first seen. He was tremulous, flushed, sweating and stammered while he spoke. His anxiety subsided rapidly after the interview began.

He immediately related feeling "nervous and apprehensive" because he blacked-out at a lower G level than he anticipated. He recalled feeling panicky and helpless soon after the run began and had felt anxious all day. He related this anxiety to statements made by two of the doctors earlier in the day. They had both reassured him that the examination was proceeding satisfactorily, and they were, in general, encouraging to him about the outcome. The patient's reaction to these statements was a feeling of apprehension because "after all, the tests weren't complete", and he wondered why the doctors made the remarks they did. He had already been concerned about the outcome of the tests and was fearful he would be told he could no longer fly. The therapist reflected the patient's discomfort about this bland reassurance. This encouraged the patient to describe feelings of anxiety which occurred whenever he was examined by doctors. It was apparent that this area had not been picked up and dealt with at all in his previous interviews.

Furthermore, the anxiety aroused when the doctors at the previous center referred him to this laboratory had never been handled. He had assumed that something must be wrong with him if he was sent here. The remarks made by the doctors earlier in the day merely enhanced his fearfulness because of two possibilities which occurred to him: 1) "something is wrong and no one can find out what it is"; 2) "my condition might be pretty serious and no one wants to describe it to me, instead they are trying to placate me." He specifically mentioned the possibility of a brain tumor since his symptoms (black-out and uncon-

sciousness) "seemed to be the kind that would result from a brain lesion." The patient had never been told the results of any of the specific tests he had, like the EEG. A general statement that everything seemed fine was made after his first workup. These concerns about a physical difficulty preventing him from flying made him particularly unhappy since it might imply that he would be permanently separated from other members of his flying group to whom he felt a strong bond of atttachment.

The therapist then asked the patient to describe the black-out incident which had occurred in flight. The patient had blacked-out three times on one flight. Each time it occurred, the instructor was flying the plane, and the patient stated he would "relax". When the patient was flying the aircraft, he was "more active" and was better able to tolerate high G-forces. When asked about the difference in feelings when he or the instructor flew, he replied, "there's always a difference. If I'm the passenger, I relax, there's nothing to do, I'm just there. All the bumps that are made, well, I'm behind the pilot and I have to follow him. When you fly you know what's happening; you can anticipate what's going to happen. I'm in control then. It's like they say when you have it, you have it. If you are a passenger, the pilot and plane are doing it. One way you're affected and the other you are doing the affecting yourself." The therapist then wondered if the patient's feelings on the centrifuge were in any way comparable. The patient stated, "It's closest to the passenger feelings, but it's a smoother ride. You can anticipate a little more what's going to happen. You can't anticipate the pilot." He then went on to relate how important a test the centrifuge was for him since it appeared to be the factor that would decide his future. The doctor's statement that he had done well the previous day might mean he "really didn't have as much control in the centrifuge" as he thought since he interpreted the reassurance to mean that he needed encouragement to perform better. He reiterated the recurrent anxieties he felt whenever he was examined by doctors even for routine "check-up's". He fears that they will test him and find something wrong, and then prevent him from doing the things he wishes to do. The only other group who produced similar feelings were his flight instructors and then only when they took him on "check" rides and not during routine flights. In a previous interview, the patient described his father as being strict and requiring that he do things in a certain way. If he failed, he would be punished by being deprived of something he desired. He stated he respected his father but could never really feel close to him because of this. He felt that it was the implication of a test situation which was so anxiety-provoking to him. It is interesting that one of the doctors had reassured him after completing an intra-arterial blood pressure reading. This reassurance coming at a time when he was being tested (and attacked) carried with it the implication that the statement was as much as an instruction to perform better as an encouragement. This was made more apparent when the patient described becoming anxious over the second centrifuge ride (where he blacked-out at low G). It seemed like a "re-test" even though he had previously been informed he would have 3 runs.

The therapist interpreted his fear of having an authority figure discover a physical inadequacy and prevent him from attaining his wishes. Following this, the therapist focused on the realistic fact that his body was able to tolerate high G levels and that his black-out was due in part to his being anxious. This was an attempt to help the patient integrate what he had already verbalized. However, the patient had concerns about whether "all this was due just to anxiety." This was picked up to mean, in part, that he was disturbed about the implication of mental symptoms. The therapist reflected this and then pointed out the vascular changes accompanying anxiety and the universality of this phenomenon in all pilots. The patient appeared tremendously relieved at this point.

The therapist then decided to encourage the arousal of aggressive, controlling, self-confident feelings by stating that he did feel the patient had a high G-tolerance and was able to control aircraft. The therapist then related the patient's black-out on the centrifuge to the same factors causing black-out

in aircraft, i.e., the passenger feeling of not being in control. The patient then brought up fears he had that something might be wrong with him, and then it would be dangerous for him to fly. He vigorously agreed to the therapist's reply that he "valued his life more than flying, and that he was concerned lest we do not do an adequate work-up and fail to find a physical difficulty he might have."

It was felt that the patient was suggesting his fear of being harmed or attacked by authorities, e.g., doctors. Neglect would then be equivalent to attack and might lead to his being injured. When he was being tested or examined by an authority, his fears of being inadequate were aroused—in addition, his being inadequate would mean he could not defend himself. His anxiety on "check" flights and on the centrifuge was related to not being in control or able to defend himself. This was, of course, tied up with his fear of being aggressive with authority figures and led to his submitting and "relaxing," thereby making him vulnerable and hence more anxious. The therapist emphasized that the main interest of the doctors was to protect and help him by being sure he could safely undertake high-speed flight. They felt that he could tolerate this and fly without danger. The therapist felt that flying and the aircraft were channels through which a tremendous amount of aggression was released. However, in a test situation (check flights) he became fearful, and this fear was related to his being harmed or overcome so that he repressed aggressive impulses. Thus, at the end of the interview, the therapist tried to reduce the patient's anxiety regarding the doctors and their motives by working through some of the unconscious sources. Thus by supporting and accepting his wish to fly (and it's aggressive connotations), the therapist hoped to stimulate the arousal of an aggressive, controlling attitude on the centrifuge.

Immediately following the interview, the patient returned for a second centrifuge run. During this series of runs, he was accelerated to 4.2 G (high G), and though he lost some peripheral vision, he did not black-out completely at even this high "G".

Discussion

It has been pointed out that the black-out threshold is dependent on cardiovascular reflex activity and can be influenced by affect state variations. This case demonstrates how a change in affect state can directly alter a person's resistance to cardiovascular stress. Furthermore, it points out the advantage of identifying the specific determinants of anxiety and dealing with them in as focused and individual a manner as possible. The determinants of anxiety in this case were both conscious and unconscious. In addition, present fears were fused with past ones.

Anxiety can be considered a signal of danger to the organism. However, the danger may not be represented in the inherent nature of the external stimulus, but often the association of past dangers not realistically represented in the present situation is more significant. Anxiety is associated with various physiological responses. The nature of the somatic reaction is based on the entire psychophysiologic pattern related to the preparation for defense or flight. This may be unrelated to the source of the danger whether it be real or fantasy.

In this case, there was anxiety aroused which was related to recent events. There was also re-activation of past conflicts, and anxiety developed which was usually handled by the patient's defenses. This anxiety was inadequately handled by the personnel examining the patient.

In formulating the therapeutic approach to this patient, the limitation of time necessitated setting a limited goal. Because of the intensity and the nature of the anxiety mere ventilation was not believed to be adequate. Furthermore it did not appear sufficient to just elicit the conscious sources of anxiety and ameliorate these by reassurance and the presentation of reality factors. It appeared important to explore the meaning of the centrifuge, flying, and relationships with instructors, doctors (and authority figures) and relate these to past determinants. The reason for this approach was the overwhelming nature of the anxiety which did not appear to be appropriate to the external threat. Although the aim of therapy was primarily ego

supportive, it appeared necessary to help the patient gain some insight into the irrational nature of his fears since these elements had already erupted into consciousness.

The patient was encouraged to release conscious affects and helped to work through these feelings. The reintegration of his ego defenses was further aided by constantly refocusing on realistic aspects of the environment and his own physiologic capacities. When it was felt that some degree of integration had been attained, attempts were made to encourage his use of substitutive and displacement mechanisms to express agression. It was hoped that by reducing anxiety in the vulnerable area and increasing his ability to release aggression, his psychophysiologic state would be altered.

It was felt that anxiety and aggression were significant affective determinants in influencing neurohormonal and physiological mechanisms responsible for G-tolerance variations. It is interesting that Von Euler (3) has already demonstrated that pilots have higher nor-adrenaline and lower adrenaline levels than passengers (who are flying personnel). This is meaningful in terms of the patient's description of his behavior and feelings in these two situations (pilot and passenger). Of course, it is not implied that the difference in affective tone is the only determinant of the differential release of adrenaline and nor-adrenaline. The muscular component of aggressive, active, controlling behavior as opposed to the more rigid, immobile, inactive state associated with anxiety may be involved. The latter state enhances the vasodilatory effects of adrenaline.

It should be pointed out that there are several possible explanations for this patient's black-out:

1) Acute anxiety and low level of aggressive feelings and behavior may result in high levels of adrenaline and reduced levels of nor-adrenaline. The hydrostatic effects of centrifugation resulting in the pooling of blood in the abdomen and lower extremities might be enhanced by the peripheral vasodilating action of adrenaline, and low nor-adrenaline levels might be associated with sluggish cardiovascular activity.

2) It is conceivable that the presence of acute anxiety could be associated with central nervous system arousal sufficient to disturb perception and result in disorganized and goal directed behavior. Hence, the patient would be able to see but would not be able to respond to the centrifuge signal lights. This would constitute a non-cardiovascular "black-out".

3) Extremely high levels of adrenaline might cause the blocking of neural impulses in the optic pathways (5). This explanation is unlikely since the levels necessary to cause this in animals appear in excess of what would be expected in anxious humans.

4) Acute panic could lead to a massive de-differentiated diffuse reaction with parasympathetic discharge and hence decreased pressor responses. However, the physiological recordings during centrifugation did not indicate this.

The initial "black-out" described in this case probably involved elements of both extreme arousal and circulatory inadequacy. However, the affect-stress response relationship seems rather clear in view of the subsequent events.

By attempting to alter his affect state in a specific and focused manner, that is, to reduce the level of anxiety and enhance the expression of aggressive impulses, his tolerance to centrifugal stress increased. It is believed there was a change in his psychophysiologic state which altered his physiologic responsivity.

Summary

The influence of specific emotional factors on cardiovascular responses to the human centrifuge is reviewed. A case is presented in which the patient's tolerance to centrifugal stress is lowered because of acute anxiety. The therapeutic approach used to alter his affect state is described. The amelioration of anxiety and the arousal of aggressive feelings result in an increase in his cardiovascular stress tolerance. The relationship of central nervous system, vascular and neurohormonal mechanisms to affect state changes is discussed.

BIBLIOGRAPHY

1. Basowitz, H., Persky, H., Korchin, S. J., and Grinker, R. R.: *Anxiety and Stress*. New York: McGraw-Hill, 1955.
2. Cohen, S. I., Silverman, A. J., and Zuidema, G.: Physiologic stress response evaluation with focused interviews. *Arch. Neurol. & Psychiat.* (In press).
3. Euler, V. s., V.: Noradrenaline. American Lecture Series No. 261, Springfield, Illinois, Charles C Thomas, 1956.
4. Goodall, McC., and Meehan, J. P.: Correlation of "G" tolerance to urinary adrenaline and nor-Adrenaline. *Fed. Proc., Am. Physiol. Soc.*, Sept., 1956.
5. Marrazzi, A. S.: Cholinergic excitation and adrenergic inhibition common to peripheral and central synapses. In *The Biology of Mental Health and Disease*. New York: Paul B. Hoeber, Inc., New York, 1952, pp. 376–383.
6. Silverman, A. J., and Cohen, S. I.: Psycho-physiologic aspects of experimental cardio-vascular stress. USAF Technical Note (WADC TN 56-396, AD 97274).
7. Silverman, A. J., Cohen, S. I., and Zuidema, G.: Psycho-physiological investigations in cardio-vascular stress. *Am. J. Psychiat.* (In press).
8. Zuidema, G., Silverman, A. J., Cohen, S. I., and Goodall, McC.: Biochemical and psychologic correlates of vascular responses. *Fed. Proc., Am. Physiol. Soc.*, Sept., 1956.

SEIZURES WITH PROMAZINE

Preliminary Report[1]

JOHN F. KURTZKE, M.D.

Promazine[2] is a phenothiazine derivative similar to chlorpromazine in pharmacologic properties, but it is said to show less evidence of acute or chronic toxic effects in equivalent doses (6). Seizures occurring as a complication of this therapy *per se* have not been reported. Initial doses utilized have varied from 50 to 400 mg., by mouth, intravenously, or intramuscularly, with later dosage of 200–1,200 mg. a day, usually by mouth (1). This report is prompted by the occurrence of grand mal fits in patients receiving promazine.

Methods and Material

At the V.A. Hospital, Coatesville, Pennsylvania, promazine was given to a total of 21 chronic psychotic patients between May 25, 1956, and Sept. 5, 1956. Observations were terminated Dec. 26, 1956.

The subject patients comprised 19 with schizophrenic reactions, one with psychotic depression, and one with general paresis. All were male; there were four Negroes. At the onset of promazine therapy, these patients had been hospitalized here for an average of 10.1 years, with illnesses having a mean total duration of 12.7 years.

The use of promazine was at the discretion of the ward psychiatrist. The initial dose utilized ranged from 75 to 300 mg. a day, except for one patient who received 900 mg. daily from onset. In all but one case, administration was *per os*, and the total daily dose was given in two or three equal parts. Ten patients received a maximum daily dose under 900 mg. a day; the remainder attained maximum levels of 900–1,800 mg./day. The amount used was also discretionary, but increased doses were necessitated by lack of improvement at prior levels.

Complicating medical factors included three patients (#6, 9, 17) with mild diabetes mellitus, one (#16) with adequately treated late latent lues, and one (#3) with chronic simple glaucoma. One diabetic received protamine zinc insulin, and patient #3 pilocarpine eye drops during this study.

Patient #13 had grand mal since 1946, averaging five to fifteen fits annually, and was taking diphenylhydantoin and phenobarbital. His EEG, mildly abnormal, was the only one not within normal limits of the 17 patients who had had such an examination within seven years of the study. No other patient had prior seizures, all had normal skull x-rays and otherwise normal blood counts, chemistries, serology, urinalyses and EKG's. Of the 11 cerebrospinal fluids examined all were normal except that in the paretic, which had been essentially negative for over 10 years. Only the paretic had an abnormal neurologic examination.

One patient (#9) had had a lobotomy (bifrontal, 1950); in only two (#13, 19) was there a history of head injury. No patient had a family history of convulsions.

Further details concerning these patients are summarized in table 1. Included are data concerning other concomitant ataractics. No regular medication was used in these patients except as noted herein.

Observations

There were no untoward effects from promazine in these patients except for the occurrence of 11 seizures in six patients (29 per cent incidence). These were all typically grand mal in nature.

Following is a brief summary of these cases.

Case 9: White male, 39 years of age, had the onset of a paranoid schizophrenic reaction in 1947. He was continually hospitalized here since Jan., 1948. In 1948 he received 53 insulin treatments and 57 more in 1949. Also in 1949 he had a course of 33 electroshock treatments and 13 more in 1950. In April, 1950, his EEG revealed an S1 pattern. In May, 1950, a standard bifrontal lobotomy was performed without untoward effects. Pre- and post-operative psychologic tests revealed no "organic" deterioration. In 1955 he received 50 mg. chlorpromazine IM almost daily.

On May 25, 1956, he was described as verbally

[1] From the Neurology Service, V. A. Hospital Coatesville, Pennsylvania.

[2] Promazine used herein supplied as Sparine by Wyeth Laboratories, Philadelphia, Pennsylvania.

TABLE 1.—Summary of 21 Patients Given Promazine

All patients male veterans

Case No.	Race	Diagnosis	Date onset, year	Present age during Rx	Adm., mo./yr.	Promazine Therapy—1956								
						Date onset, mo.-d.	Dose onset, mg./d.	Dose max., mg./d.	Days total Rx	Days max. Rx	Seizures			Clin. change
											No.	Date	Dose, mg./d.	
1	W	par. sx.	1943	50	9/51	6-25	100	100	66	66	0	—	—	I
2	W	heb. sx.	1924	59	4/33	6-20	200	200	66	66	0	—	—	U
3	W	psy. depr.	1928	59	11/32	7-18	100	200	49	46	0	—	—	U
4	W	par. sx.	1938	60	3/38	6-27	200im	200im	60	60	0	—	—	U
5	W	par. sx.	1949	50	6/50	7-2	100	600	65	40	0	—	—	W
6	W	par. sx.	1934	60	11/38	7-10	200	800	64	28	0	—	—	U
7	W	und. sx.	1942	46	3/44	6-19	100	400	68	60	0	—	—	U
8	W	GPI	1931	61	11/32	7-18	100	200	42	39	0	—	—	U
9	W	par. sx.	1947	39	1/48	5-28	150	1800	93	43	1	8-29	1800	U
10	W	cat. sx.	1946	38	5/46	6-15	75	900	77	46	0	(1 on 10–10)		U
11	W	par. sx.	1943	43	7/49	6-12	150	1800	54	12	1	8-5	1800	U
12	W	heb. sx.	1948	32	11/48	6-12	75	1200	80	40	0	—	—	U
13	W	und. sx.	1950	39	10/55	7-11	200	200	51	51	0	—	—	U
14	W	par. sx.	1946	37	10/46	6-1	300	1200	91	76	0	—	—	I
15	W	heb. sx.	1944	35	2/46	5-25	150	1200	82	56	4	6-10	1200	U
												6-25	1200	
												7-3	1200	
												7-30	1200	
16	Ng	und. sx.	1953	26	8/54	5-29	150	1500	80	7	2	7-18	1500	U
												7-30	1200	
17	W	par. sx.	1942	37	7/46	7-17	75	300	44	32	0	—	—	U
18	Ng	par. sx.	1953	33	2/54	5-29	900	1500	94	48	0	—	—	U
19	Ng	cat. sx.	1950	27	10/52	6-14	150	1200	78	49	1	8-30	1200	U
20	W	cat. sx.	1943	39	4/45	6-14	150	1200	29	3	2	6-26	900	I?
												7-15	1200	
21	Ng	par. sx.	1954	28	7/55	5-24	150	1500	95	13	0	—	—	I
												(400 mg. last month)		

Legend:

Ng—Negro	par. sx.—paranoid schizophrenia	im—intramuscular
W—white	heb. sx.—hebephrenic schizophrenia	I—improved
Rx—therapy	cat. sx.—catatonic schizophrenia	U—unchanged
d.—day(s)	und. sx.—undifferentiated schizophrenia	W—worse
mo.—month(s)	psy. depr.—psychotic depression	clin.—clinical
yr.—year(s)	GPI—general paresis	

ECT		IST		Prior ataractics type, dose in mg./d	Prior EEG	Promazine EEG	Other Rx—on promazine	Case No.
Total No.	Years	Total No.	Years					
15	'45	34	'46	Th. '55—shock	N	—	0	1
0	—	0	—	0	N	—	0	2
37	'51–53	0	—	Th. 400, res. 4	N	—	mepr. 800	3
0	—	0	—	Th. 100 im	—	—	0	4
49	'49, 52	129	'50–51	Th. 1000	N	—	0	5
0	—	?	'39	Th. ?	—	—	0	6
184	'49–55	57	'49	res. 6	—	—	res. 6	7
0	—	0	—	0	N	—	0	8
46	'49–50	110	'48–49	0	N (S1)	—	0	9

TABLE 1.—*Continued*

ECT		IST		Prior ataractics type, dose in mg./d	Prior EEG	Promazine EEG	Other Rx—on promazine	Case No.
Total No.	Years	Total No.	Years					
65	'47–49	103	'47–48	Th. 300, res. 10	N	—	res. 2, Rit. 60	10
40+	'43, 46, 52	53	'49	res. 4	N	abn (cf. text)	0	11
0	—	164	'48–51	Th. 50—shock	N	—	0	12
0	—	0	—	Th. 100	abn (S2)	—	0	13
33	'46–52	75	'46, 48	Th. 100, res. 2	N	—	0	14
8	'44	58	'47	Th. ?	—	abn (cf. text)	0	15
?	'53	58	'54	0	N	N	0	16
93	'46–53	57	'47	Th. ?, res. 8, mepr. 1800	N	—	res. 10 Rit. 60	17
0	—	58	'54	Th. 600	N	—	Rit. 60	18
12	'53	56	'52, 53	0	N	abn (cf. text)	Rit. 80	19
69	'45–49	56	'47	0	N	N	Rit. 60 added 7–13	20
16	'54	0	—	Th. 800	N	—	Rit. 80	21

ECT—electroshock therapy
IST—insulin shock therapy
'51–53—1951 to 1953
'49, 52—1949 and 1952
40+—one course of 40, plus other course(s), no. unknown
N—normal
abn—abnormal
Th. 400—chlorpromazine 400 mg. total daily dose
res. 4—reserpine 4.0 mg. total daily dose
mepr. 800—meprobamate 800 mg. total daily dose
Rit. 60—Ritalin 60 mg. total daily dose
Th. ?—chlorpromazine, dose unknown

threatening, silly, occasionally demanding, passively cooperative, occasionally untidy and exposing himself, and with inappropriate laughter. Promazine, 50 mg. t.i.d., was started on May 28 and raised gradually to 400 mg. t.i.d. by June 13; on July 13, 500 mg. t.i.d. were begun and four days later changed to 600 mg. t.i.d. On Aug. 29 he suffered a typical grand mal seizure lasting three minutes. Neurologic examination was normal the next day. Promazine was discontinued Aug. 31, at which time there was noted no change in the clinical status described above. There have been no further fits.

Case 11: A 43-year-old white male, hospitalized since July, 1949, for a paranoid schizophrenic reaction with onset in 1943, had received 40 ECT and 53 IST in 1952 and 1949, respectively. Before this hospitalization there had been two other courses of electroshock, in 1943 and 1946. He was given 4 mg. reserpine from April, 1955, to onset of promazine therapy on June 12, 1956. On that date he was described as tense, hostile, emotionally unstable, suspicious, aggressive and delusional.

Promazine, begun on June 12 at 50 mg. t.i.d., was raised to 300 mg. t.i.d. by June 20 and 600 mg. t.i.d. on July 24. On Aug. 5 he had a severe grand mal with clouded consciousness for three hours post-ictally. Repeated neurologic examinations over the ensuing week were normal. The drug was discontinued on Aug. 5. EEG on Aug. 7 showed a predominant frequency of high amplitude 5–7 per second waves with bursts of 3–5 per second, the latter of greater amplitude on the right side anteriorly. Pre-shock EEG in 1949 was normal. There was no change in his clinical state on promazine; there have been no further seizures.

Case 15: This white male of 35 was hospitalized since Feb., 1946, for hebephrenic schizophrenia with onset in 1944. He received 8 ECT in 1944 and 58 IST in 1947. He had had a course of chlorpromazine in 1955. On May 25, 1956, he was considered untidy, sloppy, hostile, negativistic, preoccupied, withdrawn, hallucinating, and an eloper. On that date promazine, 50 mg. t.i.d., was started and raised gradually to 400 mg. t.i.d on June 5. On June 10 he had a short grand mal. The drug was discontinued for two days and reinstituted then at same dosage. On June 25 he had a second major seizure. EEG on June 29 showed high amplitude 9–10 per second background with a large amount of random 4–5 and 5–7 per second waves, plus many 1–2 second seizure discharges. On July 3 and 30 he suffered his

third and fourth convulsions. On July 31 promazine was lowered to 300 mg. t.i.d.; on Aug. 2, EEG revealed predominant 8 per second waves with bursts of 5 and 3–4 per second activity, with a marked buildup on hyperventilation. Promazine was discontinued Aug. 15, and reserpine 8 mg. begun on Aug. 31. EEG on Sept. 6 showed normal alpha record with occasional bursts of 6–7 and 4.5–5 per second waves; hyperventilation gave no response. There have been no further seizures. Repeated neurologic examinations during this period were normal. Clinically there was recorded no change or possible worsening while receiving promazine.

Case 16: This 26-year-old Negro, hospitalized August, 1954 for an undifferentiated schizophrenic reaction with onset the previous year, had received a course of ECT in 1953. In 1954 he was given 58 IST combined with 16 ECT. A positive blood serologic test for syphilis was discovered in 1952, and he has been given three courses of penicillin since then. Spinal fluid was normal in 1952, 1954, and August, 1956. Blood serology has remained positive. Neurologic examinations on admission and August, 1956, were normal.

On May 29, 1956, he was noted to be preoccupied, indifferent, withdrawn, blocked, negativistic, manneristic, and responding to hallucinations. On that date promazine, 50 mg. t.i.d., was instituted and gradually increased to 500 mg. t.i.d. by July 14. On July 18 he had a typical grand mal convulsion. On July 21 promazine was lowered to 400 mg. t.i.d. EEG's in 1954 and on July 25, 1956, were perfectly normal. On July 30 the second seizure occurred, and the next day promazine was reduced further to 300 mg. t.i.d., and completely discontinued Aug. 17. There was no clinical change; there have been no further seizures.

Case 19: A 27-year-old Negro was hospitalized since October, 1952, with a catatonic state beginning in 1950. In the 1952–53 winter he had a course of 56 IST with 12 ECT. In 1944 he fractured his jaw in falling off a ladder but was not unconscious. On June 14, 1956, promazine, 50 mg. t.i.d., and Ritalin, 20 mg. t.i.d., were begun, at which time he was preoccupied, indifferent, withdrawn, negativistic, suspicious, hallucinatory and blocked. On July 13 he had been raised to 1,200 mg. promazine and 80 mg. Ritalin. On Aug. 30 he had a grand mal fit of three minutes' duration. The next day both drugs were discontinued, and 8 mg. reserpine started. EEG of Oct., 1952, was normal; EEG on Sept. 5, 1956, showed a predominant frequency of high amplitude 6–7 per second waves with bursts of 4–5 and some 3–4 per second activity more marked over the left hemisphere anteriorly. There have been no further fits. There was no clinical change on promazine.

Case 20: This white male, now 39, has been hospitalized here since 1945 for catatonic schizophrenia with onset in 1943. He was given 19 ECT in 1945, 38 in 1948–49, and 56 IST with 12 ECT in 1947. On June 14, 1956, he was described as preoccupied, slovenly, negativisitic, mute, tense, fearful, withdrawn, indifferent. On that date promazine, 50 mg. t.i.d., was started and raised gradually to 300 mg. t.i.d. on June 21. On June 26 he suffered his first grand mal convulsion. EEG's of 1950 and July 6, 1956, were normal. On July 13 promazine was raised to 400 mg. t.i.d. and Ritalin, 20 mg. t.i.d., added. On July 15 his second major fit occurred, and promazine was stopped the next day. Ritalin was continued at 20 mg. b.i.d. and reserpine 8 mg. added. On promazine there was no clinical change although it was noted he "mumbles a few words". No further seizures ensued.

Possibly pertinent to the problem was the following case:

Case 10: A 38-year-old catatonic schizophrenic in hospital since onset in 1946 had had 46 IST with 6 ECT in 1947, 57 IST with 21 ECT in 1948, and 38 ECT in 1949—with no spontaneous seizures and negative prior history for same. EEG Sept., 1955, was normal. He had received chlorpromazine in 1955 and reserpine 10 mg. for the two months preceding promazine. He was mute, preoccupied, indifferent and withdrawn when promazine, 25 mg. t.i.d., was instituted June 15, along with reserpine 4 mg. and Ritalin 60 mg. From July 16 to Aug. 31 promazine dosage was 300 mg. t.i.d. On Aug. 31 promazine and Ritalin were stopped and chlorpromazine added. On Sept. 28 ECT was begun and on Oct. 10, two hours after a shock treatment (his 6th), he suffered his first and only grand mal seizure.

Of interest also was the following patient:

Case 13: A 39-year-old undifferentiated schizophrenic since 1950 was admitted October, 1955. He has had grand mal since 1946, averaging five to 15 fits annually. There was a vague history of head injury with concussion while a prisoner of war in 1943. Skull x-rays, pneumoencephalogram, spinal fluid were normal. Two neurologic examinations in 1956 were normal. Psychologic tests revealed no evidence of brain damage but marked signs of an active schizophrenic process. On July 11, 1956, he was described as oriented, coherent and relevant, but had previously been tense and assaultive. From that date to Aug. 31 he was given promazine, 100 mg. b.i.d. During this period there were no fits, although he had to that time had 15 seizures since admission. However, his diphenylhydantoin had been raised from 0.2 to 0.4 grams daily at the beginning of July, while his phenobarbital 0.03 grams was maintained.

Discussion

In a period barely exceeding two months, six patients out of a total of 21 given promazine exhibited 11 grand mal seizures, and have had none in the ensuing four months after cessation of the drug. These patients were all psychotic and had been hospitalized an average of 10 years in the same institution. Excepting the patient with grand mal, there had been no seizures in the previous 2,500 patient-months of hospitalization, while in 48 patient-months on promazine, 11 fits had occurred; in the next

TABLE 2.—COMPARISON OF PATIENTS WHO HAD SEIZURES WITH PROMAZINE WITH PATIENTS NOT HAVING SEIZURES WITH PROMAZINE

Factor	Six Pts. with fits		Fifteen Pts. without fits		t*	Significance
	Mean	Range	Mean	Range		
Duration of illness (yr.)	9.5	2–13	14.1	2–32	1.163	not sign.
Age at promazine Rx	34.8	26–43	45.9	28–61	2.128	barely sign. (5% level)
Hospital stay (yr.)	7.0	2–11	11.3	1–24	1.217	not sign.
Maximum dose promazine (mg./day)†	1450	1200–1800	630	100–1500	3.67	highly sign. (beyond 1%)
Duration promazine Rx (days)	69.3	29–93	67.4	42–95	—	not sign.
Duration maximum promazine Rx (days)	28.3	3–56	46.7	13–76	2.033	not sign.

* t^2 is $\frac{(\text{difference between means})^2 \times N_1 \times N_2}{\text{variance of measurements} \times (N_1 + N_2)}$

For n of 19, P is 0.05 at t of 2.09, 0.01 at t of 2.86.

† Maximum dose was also dose at which seizures occurred in all patients, with (in two) fits at lower doses in addition.

80 patient-months, only one seizure took place. This last happened two hours after an electroshock treatment and 40 days after cessation of 1,200 mg. promazine, without convulsions during drug therapy.

Due to the fact that this was an unexpected development, no "clean" study was possible, so that some patients were receiving other ataractics, and most had had prior ataractics, electroshock, and/or insulin therapy. In addition laboratory studies—especially pre- and post-treatment EEG's—were lacking in part.

Although these patients varied in a number of factors (some of which are summarized in table 2), a most significant difference was found in the average maximum dose (P less than 0.01) when the group was divided into those who did and those who did not have seizures. Maximum dosage averaged 1,450 mg./day (range 1,200–1,800) for those with fits, although one patient had his first convulsion on but 900 mg.; those without seizures had an average maximum dose of 630 mg./day (range 100–1,500). No patient had a convulsion when his maximum dose was under 900 mg.[3]; this included the patient with grand mal (whose anti-convulsants had coincidently been increased) and the patient with general paresis (inactive for more than 10 years).

As to the coincident medication, reserpine was used in three patients and meprobamate in one—none of whom had seizures. Ritalin,[4] an "anti-depressant", is said to be possibly epileptogenic (4) although Ferguson (2) reported no seizures in a group of senile patients given this agent. Ritalin in the present study was administered to four patients who did not and two who did have convulsions; of the latter, one received Ritalin for the first time after his first convulsion on promazine, while in the other its use was coterminal with promazine. It therefore seems most unlikely that these other agents were responsible for these seizures; also these drugs are in widespread use throughout this hospital, and thus far there has been no alteration in seizure incidence associated with any other ataractic, in the dose-range employed. In fact, but 43 (3.3%) of the 1,300 schizophrenics hospitalized here have had any seizures. Fifteen had but one or two during insulin or electroshock, two had one each shortly after lobotomy, and one had a single seizure shortly after a skull fracture. Therefore,

[3] Chi-square (Yates) for incidence of fits in patients with under 900 mg. vs. 900 mg. + was significant with P less than 0.05 (χ_c^2 was 5.02).

[4] Ritalin HCl (methylphenidyl acetate HCl).

only 25 (1.9%) of the schizophrenics here may be considered seizure patients. Consequently this sudden flurry of seizures in patients receiving promazine was not in keeping with previous experience.

The prior use of physiologic therapies also does not seem to be of import since so ıe 80 per cent of schizophrenics in this hospital had been treated in this fashion. It should be noted that none of these patients receiving promazine had had any such measures within two years of drug therapy, and in most these procedures were even more remote.

Insofar as the EEG is concerned, there are treatment tracings on only five patients, all having had seizures with promazine. Two of these were normal with no change over pretreatment records. Two showed treatment records which were paroxysmally abnormal, as against prior tracings which were normal. The fifth had no previous EEG, but serial tracings with cessation of drug use showed a reversion toward normal from one pathognomonic for seizure discharges.

We come then to the tentative conclusion that the seizures reported above are associated with no demonstrable factor other than the use of promazine and—thus far—with high doses of promazine.

Of interest is the comment by Shea (7) that "In one patient, . . . the intravenous administration of 750 mg. of promazine was followed within 3 to 4 minutes by a typical grand mal seizure." (p. 227). This patient had delirium tremens but no fit other than the one with promazine. Fazekas (1) reported 11 patients with seizures of 110 cases of delirium tremens, treated with promazine in dosages probably under 1.0 gram a day.

Seizures have also been reported with the chlorine derivative of promazine (Thorazine). Schlichter (5) stated that of 21 patients, 11 had 14 seizures during chlorpromazine therapy; nine of whom while on doses of 1,200–2,900 mg./day. In his opinion, the seizures with chlorpromazine are due to hypoxia secondary to postural syncope. In the present series such a causation does not appear likely since 1) several patients of this group have had prior shock with small doses of chlorpromazine—without seizures; 2) syncopal episodes due to hypotension are relatively common—without seizures; 3) the patients receiving promazine did not have hypotension—with or without seizures. All the seizure patients had blood pressure readings in the post-ictal state, and most patients had intermittent blood pressure recordings throughout therapy. This is in accord with Mitchell's experience with promazine (3), that "Little hypotensive effect was seen . . ." (p. 45), although Fazekas (1) intimated some hypotensive effect was present, at least in some alcoholics.

It may be noted that the lower part of the dose-range employed in Schlichter's work with chlorpromazine corresponds with the doses of promazine at which seizures occurred in the present report. This dosage was necessitated by the lack of clinical improvement at lower levels. Even with these doses, only three patients were said to have improved: one (#1) at 100 mg. daily, one (#14) at 1,200 mg., and one (#21) at 1,500 mg. These patients may well have been relatively poor choices to test the adequacy of a drug; they were on the whole chronically and severely ill patients who had not responded to most of the measures previously available. However, as a group such patients comprise a large part of our hospital population; it is from this category (among others) that hopeful reports have been written concerning ataractic medication; and, while this report is not primarily concerned with the efficacy of this agent, it is apparent that it has a direct bearing on the question of seizures. For if fits were produced with 2,000 mg. promazine, and clinical improvement took place at 1,000 mg., their occurrence would be academic; but not with the converse.

It is essential to study further the effects of this agent to determine 1) is promazine actually epileptogenic? 2) if so, is it solely a function of dose-level? 3) if this dose-level is not above usual therapeutic ranges, will anti-convulsants be of use? Further correlations with diagnosis, age, and improvement—among others—are also necessary. And some hints as to mode of action may arise.

Summary

1. Twenty-one chronic psychotic patients were given promazine over an average period of 68 days, with maximum doses ranging from 100 mg. to 1,800 mg. a day.

2. Of this group, six patients experienced a total of 11 grand mal seizures during promazine therapy. All these patients were receiving 900 mg. daily or more at the time of the convulsions.

3. Five patients also administered 900 to 1,500 mg. a day did not have seizures during therapy.

4. No patient of the 10 receiving less than 900 mg. daily had fits.

5. In three patients with clinical fits with promazine, serial EEG tracings showed paroxysmal records during drug use only; in two others with seizures, a normal record was found with and without the drug.

6. It is concluded that in this series. the administration of high doses of promazine was associated with the occurrence of grand mal convulsions.

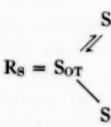
BIBLIOGRAPHY

1. Fazekas, J. F., Schultz, J. D., Sullivan, P. *M.*, and Shea, J. G.: Management of acutely disturbed patients with promazine (Sparine) *J. A. D. A. 161:* 46, 1956.
2. Ferguson, J. T., and Funderburk, W. H.: Improving senile behavior with reserpine and ritalin; new approach with use of methyl phenylpiperidylacetate. *J. A. M. A., 160:* 259, 1956.
3. Mitchell, E. H., Treatment of acute alcoholism with promazine (Sparine). *J. A. M. A., 161:* 44, 1956.
4. Morpurgo, C. V.: Clinical observations on a new substance with central stimulating effect (abstr.). *J. A. M. A., 161:* 1514, 1956.
5. Schlichter, W., Bristow, M. E., Schultz, S., and Henderson. A. L.: Seizures occurring during intensive chlorpromazine therapy. *Canad. M. A. J., 74:* 364, 1956.
6. Seifter, J., Begany, A. J., Huber, R., and Bruce, W. F.: Wyeth Institute for Medical Research data. (To be published.)
7. Shea, J. G., Ehrmantraut, W. R.. Ticktin, H. E., Sullivan, P. D., Jr., and Fazekas, J. F.: Use of promazine in the management of medical emergencies. *Mil. M. J., 119:* 221, 1956.

CRITERIA FOR TRANQUILIZATION AND THE WELL-BEING STATUS OF SUBJECTIVITY

PHILIP SNELL, M.D.

Stress analysis[1] (4) does not propose to lay words in the way of practical accomplishment. It is a predetermined empirical arrangement of clinical experience for the acceptance of the experimental facts relative to inhibition and facilitation of the peripheral and cortical synapse. It deals through the interpretation of symptom complex phenomena with a fundamental characteristic of the behavioral nature of the neurogenic tissue and its reflexivity which cannot be ignored or by-passed by the more familiar statistical clinical correlations. The reflexivity of symptom complex is viewed as dynamic from the evidence of clinical reversibilities of phenomena. Although the neurogenic tissue balance may be altered by metabolic deficiency of diverse etiology, referred to as endocrine deficit, its reflexivity phenomena are evidence of its stress, by adopting patterns not usually a part of subjectivity and the well-being status. The schematic which depicts the composite of this reflexivity at its gross levels of integration emphasizes the non-specificity of the neurogenic reactivity. The placebo becomes a symbol of a kind of stimulation or influence not dependent on alteration of neurogenic tissue of a vital and focally sensitive center, but that derived from neurogenic impulse and circuitry (respiratory, temperature, vomiting, cortical sensory and psychic, etc.). A delineation of influence of these vital areas on the reflexivity status of subjectivity is a prime purpose with stress analysis.



The reflexivity levels of registration:
Stress (S)
Cortical (C)
Optic thalamic (OT)
Peripheral (P)

[1] Synonymous term for conduction analysis.

The schematic depicts the unit of physiologic reversibility from which is derived the meaning or significance of the pertinent clinical and theoretic factors.

Thus the analysis of clinical phenomena of inward tension or associated phenomena by respiratory stimulus (R_S) displacement or analgesic blocking (=) at the theoretic synapse creates an opportunity of comparison of pharmacological therapeutic agents on the basis of reflexivity symptom complex reversibility. Regardless of the manner of known pharmacological tissue influence or stimulus replacement (=) of endocrine deficit ($R_S = E$) in neurogenic tissue, a standard of comparison is feasible. The intensity of the physiological stress involved in inward tension states, e.g., as revealed by stress analysis, may in no way be satiated by the pharmacological agent within its particular toxicity limits. Aside from this possibility of individual idiosyncrasy and tissue toxicity, the whole problem of tranquilization needs to be viewed realistically from the aspect of physiological tissue interference and the reflexivity approachable by stress analysis.

The objective of tranquilization of a particularly troublesome emotive phenomena (e.g., inward tension) with its intimate neurological reflexivity association brings it within positive range of comparison of intensities of stimulus and stress involved. If the general experience finds a particular agent of a milder degree of effectiveness, obvious conclusions on the basis of stress analysis with respect to alternative choice of phenomena blockade may be derived, enabling an appraisal of intensity and responsiveness to be clinically correlated.

Although physiological stress displacement and tissue interference may be fundamental to reversibility of symptom complex at a particular period of time, the pertinent matters of individual recognition and interpretation (auto suggestion, instructive persuasion) may easily decide the adjunct nature of the deliberate stress displacement with respect to the whole aspect of psychotherapy.

The element of psychotherapy in stress analysis may be viewed from the aspects of stress registration and the physiological response to the phenomena blockade (by various agents, placebo, etc.); their behavioral facilitation or resistance conveys some measure of the synaptic tissue disturbance. Stress analysis may also interpret the meaning of phenomena intensification, sensitivity and resistance (physiologic and psychic blocking) which in the development of symptom complex may evolve as distinctly different considerations regarding phenomena behavior and the vital centers of function involved (respiratory, vasomotor, etc.). Extreme instances of phenomena intensification may demonstrate degrees of hypothalamic nuclear disturbance (vasomotor, vomiting, etc.), initiating functional changes such as blood pressure rise or fall, pallor or flush, sensory feeling of malaise, vomiting, fatigue, exhaustion, with perhaps many of the motor aspects of symptom complex also apparent. Resistance, too, may be complicated not only by a tenacity of physiologic stress registration, but in the dominance of certain patterns of survival and aggression which may require intensive psychotherapy. However, these considerations need not necessitate a change in procedure of stress analysis, and the placebo-inducing stimulus should receive precedence and be evaluated as clinical experience.

Instances of idiosyncrasy and specific sensitivity (allergy, pain, psychic disturbance, etc.) may be desensitized by repeated R_S stimuli and minimal psychotherapy to build up the level of tolerance (in the author's experience) and possibly avoid the imminent dangers of theoretic synaptic cholinergic paralysis of vital centers, demonstrable in the experimental model (3).

In conclusion, the disputed psychotherapeutic element can only be appraised by analysis of the symptom complex experience. The clinical impression of sensitivity, intensity and resistance is not only evidence of synaptic stress at the schematic levels of stress registration, but of tissue disturbance referred to grossly as endocrine deficit. A review of the proposed reflexivity schematic may enable a clinically useful differentiation between psychic and somatic dominated patterns, revealing the necessity and type of psychotherapy to be employed, which may range from minimal (rapport with auto suggestion) to more elaborate forms of instructive and analytic psychotherapy.

Stress analysis aids in differentiating the psychic from the somatic stress areas by indicating more positively the dominant area of influence very often betrayed by total impressions of symptom complex phenomena. The clinician has a simple and useful tool in stress analysis of symptom complex phenomena which directs him to the area or areas of vital neurologic dominance. The phenomena relative to subjectivity (alluded to with respect to inward tension) and its well-being status require a consideration of mechanism from the various points of view afforded by stress analysis which concerns itself with the nonspecific reflexivity state during the period of clinical observation.

Specific stimulations of focal areas (respiratory, temperature, hypothalamic, vomiting, etc.) create an interference in the reflexivity fundamental to subjectivity. A dehiscence or window is thereby created, with respect to predominant stress areas and the associated components sometimes revealed as release phenomena (muscle tone, emotive and vasomotor, etc.). Thus one specific phenomenon, e.g., inward tension, may possess different stimulatory points of view (R_S, T_S, $Hypo_S$, $Cortical_S$, etc.). The levels of subjectivity stress concentration must ultimately, from the clinical aspect, be regarded as the same (cortical, optic thalamic, hypothalamic, periphery). The agent or stimulus most useful to the analysis is determined by experience on an individual basis.

The interest in the hypothalamic area and in particular that concerned with pituitrin- or pitressin-like drugs is many-faceted as a review of the literature will reveal. The labile homeostasis and metabolic tissue shifts provide a window into important physiological happenings (e.g., acromegaly, diabetes, etc.).

Symptom complex labilities provide another aspect of neurogenic tissue disturbance, the clinical observation of which may lead to some speculative considerations regarding the vasomotor, emotive and muscle tone association.

This crucial stress area emphasizes the gross dramatic functionality of the viscera with an assortment of phenomena related to specific

mechanisms of nuclear function (appetite, thirst, urinary excretion, and, in the female, menstruation, etc.).

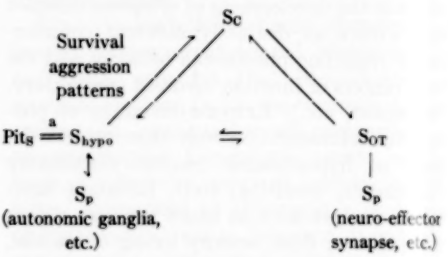
The physiological catharsis or shock syndrome triggered by the pituitrin substance may be regarded as a specific stimulant of the hypothalamic area generally, similar to pilocarpine and apomorphine, or presumed not to alter the neurologic tissue concerned (a placebo stimulus), but only its hormonal balance at synapse favoring the cholinergic or facilitation. However, this point of speculation need not be resolved solely by stress analysis.

Nuclear catharsis thus set off and the heightening of somatic punishment with a denouement or symptomatic relief (which may take place in minutes or several hours of time) may be the experience most needed by the patient to temporarily rid him of the deleterious behavior instigating psychic and somatic patterns with its accompaniment in subjectivity of extreme inward tension and other phenomena.

Symptom complex intensification by this means may also give evidence of the functional and pathologic damage of this gross anatomical area of general importance to many vague syndromes (neuro-circulatory asthenia, etc.). It may furthermore introduce a more reasonable approach to many associated clinical problems with multiple avenues of replacement of the physiological stimulus (alcoholism, addiction, neurasthenia, etc.).

The well-being status has been discussed in terms of hypothalamic stress (S_{hypo}) centers, the association of which with somatic and psychic survival patterns indicates a reciprocal relationship with cortical stress (S_C) areas and general optic thalamic stress (S_{OT}). Hypothalamic reflexivity is presumed a definite clinical component of total subjectivity via physiological neural association. The gross pattern of stress reflexivity initiated by the pituitrin stimulus and stress may be represented schematically for relevant phenomena of varying intensity. The focal phenonema of this area depict a nuclear stress relationship and are exaggerated as release phenomena.

Vasomotor phenomena suggest reciprocal stress or reflexivity relationship between peripheral ganglia of viscera and the hypothalamic nuclei. However, a reverberative circuitry ($\rightleftharpoons$) as is experimentally shown between cortical and thalamic centers is not inferred. The reciprocal impulse ($\leftrightarrow$) relationship, though doubtful from the anatomic point of view, is presumed on the basis of functional reaction and symptom complex reflexivity phenomena, elaborated later. The pituitary stimulus of aggravation or intensification referred to above may be represented as ($\overset{a}{=}$) as distinguished from the symbol ($=$) signifying stress displacement.



Both from the theoretical aspect with respect to circuitry and from the practical where rapport and cooperation are paramount, the patient's well-being status is evaluated along with the ablation of the primary stress (pain, etc.) providing somewhat indirect evidence of the importance of this gross neurological landmark with respect to the multitude of phenomena of clinical importance in symptom complex.

Although stress analysis emphasizes reflexivity, this nuclear area is involved in endocrine and general tissue function which may comprise the whole of functional pathology. This reflexivity involved in subjective symptom complex is separately delineated from that of hypothalamic function. This distinctiveness emphasizes the multiple role of the theoretic single stimulus in both symptom complex reflexivity and the neurality of peripheral function. Consequently an alcoholic and a concomitant lupus erythematous syndrome may emphasize divergent reflexivity and functional pathological aspects. The stimulus (R_S, T_S, Pit_S) portrays the reflexivity, whereas the alteration of function demonstrates peripheral neurality associated or dissociated with the former; e.g., R_S may or may not initiate the course of these events, a hypermotility of stomach with secretion diminished or increased for 10 to 15 minutes, after which a period of hypomotility may follow.

In Cushing's work (1) no singular principle is offered to describe this gross reactivity except for some few pharmacological agents (e.g., pilocarpine, etc.). Specificity so often linked to physiological function and biochemical enzyme systems cannot therefore be claimed. However, the non-specificity of neurological reactivity is clearly demonstrated and supportive to the general stress speculation, is the chance and circumstance of vital centers and circuitry which involve so many agents or stresses with similar clinical phenomena.

The area stimulus of hypothalamic and associated centers offers a point of view in the analysis of stress phenomena with a somewhat different emphasis on the vasomotor apparati (sympathetic and parasympathetic) and an association with emotive phenomena (e.g., inward tension) often in direct association with psychic and somatic patterns of aggression (appetite, sex, etc.) and survival (fear, flight and fight). Viewed clinically, the sensory motor appreciation of the well-being status (e.g., tranquillity, appetite, mental clarity and vigor, and the antithesis; inward tension, malaise, asthenia and the feeling of impending doom) may be amplified by vasomotor, emotive and muscle tone conduction dynamics and of certain patterned associations mentioned above. A spreading stimulatory impulse (R_S or T_S) need not infer that hypothalamic centers are not involved. Stress analysis which depends on intimate rapport and cooperation of the patient takes full cognizance of the well-being status, and the related phenomena may be primary or secondary, depending on the symptom complex experience and basic etiology.

In conclusion at this point, stress analysis provides an opportunity of scientific investigation of the well-being status with a consideration of a diversity of psychic influence patterns and circulatory agents. The common pathway of stress associated with this area of the diencephalon and its expressiveness is indicative of the chance and circumstance of internal and external environment with which this vital circuitry may find itself involved and which consequently presents a problem in clinical experience rather than one of anatomic cause and effect relationship. Some circulatory agents may be relied on pharmacologically for constancy of effect (e.g., apomorphine) on one or more of the sensitive nuclear centers. This observation may also hold for the anti-diuretic hormone, administered I.M. or I.V., in relation to the vomiting, vasomotor centers and others involved in the individual reaction. Although the peripheral effects of this agent may add a somewhat confusing note in analysis, the use of blocking agents (thorazine, etc. (2)) will provide analgesia to much of the nuclear stress without affecting the peripheral effects (stomach pain, contraction of uterus, defecation and voiding, etc.). This clinical demonstration should relieve the physiological doubts relative to the agent's hypothalamic action so well demonstrated by Cushing in his direct experimental studies.

A speculative promulgation of mechanism must distinguish hypothalamic function from its reflexivity. The latter are clinical demonstrations of phenomena which depict stress, whereas the former, with its vast neural ramifications, via its peripheral ganglia may influence function of a sympathetic or parasympathetic character.

The non-specific stimulus and its particular influence on the hormonal synaptic balance become an entertainment of physiological foci of stimulation (R_S, T_S, Pit_S, etc.) and pharmacological agents to which the clinical aspects of stress analysis give practical meaning.

Conclusions

A. Stress analysis offers a physiological orientation of conduction phenomena and their therapy.
   1. The psychotherapeutic means of stress abatement may receive physiological guidance.
   2. Thalamic and diencephalic anatomic and physiological considerations, from the clinical aspect, explain more fully the action of drugs employed as tranquilizers.
      (a) The well-being status of subjectivity regarded on this basis aids in the interpretation and therapy of its prominent stress phenomena.
      (b) A nuclear point of view may 1) aid in the management of many non-specific hypothalamic vague syndromes (neuro-circulatory, asthenia alcoholism, hypertension, CA, menopause, and physiological aspects of

the pathological personality, etc.) which reflect a catharsis similar to excessive pituitary extract administration with regard to the well-being status; 2) safeguard the hormonal conduction relations at synapse involved in reflexivity of vital centers (idiosyncrasy, special sensitivity, allergies, anesthesia, etc.).

3. The nuclear association of reflexivity and peripheral function may form an important therapeutic fulcrum (e.g., cardiac, gastric, vascular, etc.), considering the various stress concentration areas involved in the pathogenesis of the lesion as points of corrective intercedence (diagrams in text).

B. Stress analysis provides the dynamic criteria for the expedient use of the tranquilizing circulatory chemotherapeutic agents.

1. The placebo stimulus (e.g., R_S) and the stress stimulus (Pit_S) serve as a measure of comparison depending on the intensity and resistivity of the stress phenomena.
2. For stress phenomena (e.g., inward tension) of mild or moderate intensity, the placebo stimulus (R_S) may be a most useful tool in guiding adequate tranquilizer therapy.
3. The milder or moderate associative functional derangements (e.g., blood pressure, gastric, etc.) may show variable recovery with the use of tranquilizing agents.

C. Catharsis therapeutics (apomorphine, pituitary ext., etc.) for tranquilization or functional reversal of nuclear stress areas may perhaps be considered with procedural psychiatric shock therapies. The latter by its influence on neurogenic tissue metabolism arouses considerable doubt whether the ambulatory electric shock treatments could possibly be a substitute for the safety and expediency of controlled tranquilization by chemotherapeutic agents. The relationship of these physiological stress displacements via reflexivity or neural tissue interference to psychotherapy must be fully appreciated.

BIBLIOGRAPHY

1. Cushing, H.: *Pituitary Body and Hypothalamus.* Charles C Thomas, Springfield, Ill., 1932.
2. Freedman, D. X., and Gearman, N. J.: Apomorphine test for tranquilizing drugs. Effect of Dibenamine. *Science 124:* 264, 1956.
3. Morrazzi, A. S.: Some indications of humoral mechanisms. *Science, 118:* 367, 1953.
4. Snell, P.: Disorder in basic premise of subjectivity and placebo. *Anesth. & Analg., 35:* 495-517, 1956.

217 Paulison Avenue
Passaic, New Jersey

UNEXPLAINED MENTAL PHENOMENA REGARDING SUICIDE

R. K. GREENBANK, M.D.

The tragedy and drama of the act of suicide may cause events, which take place in persons close to the victim, to be ignored, especially if these events are mental in nature.

Suicide is well known as the acting out of intense emotional feelings. It may well be that, except for some murders, such intense feeling is never otherwise generated. This may account for psychic phenomena, such as we will discuss, occurring in those associated with the suicidal person.

First case

(A drama with a cast of three M.D.'s)

A senior surgical resident was seen by an intern, interested in psychiatry, when the resident's roommate noted he was depressed and behaving strangely as indicated by "having torn a pile of tiny bits of paper, several inches high, on his dresser." The surgical resident was foreign-trained and the son of a prominent physician in his native oriental country. He had considerable difficulty in speaking English, and understanding his spoken communications was difficult. Nevertheless, after an interview, the intern felt the resident to be suffering from an acute paranoid schizophrenic reaction. He feared injury to others, but did not think of suicide as a possibility. The case was referred to medical authorities who felt the psychiatric condition to be "homesickness". Psychiatric consultation was impractical. That night the resident asked to be left alone, saying, "I am writing a letter." The letter, written in Japanese, stated, "I am a disgrace to my profession; I have heard repeated profane and derogatory comments about me over the doctors' paging system; I, therefore, have no honorable choice open but to die." He then committed suicide by neatly slashing both femoral arteries with a surgical knife. He bled to death in his bed.

While no one consciously thought of suicide, the awareness of his plans apparently made an impression at a deeper level on at least two of the people involved.

The roommate reported a terrifying dream which awakened him from his sleep, an unprecedented experience for the resident in question. "I dreamed of a chicken with its head cut off flopping around the room; it was spurting blood all over. I was terrified."

The intern was concerned with the problem of the resident, but slept soundly until awakened at 4:00 a.m. by an emergency phone call from a hospital ward. He was consciously not considering the resident as he walked down the hall past a large, bright red coca cola machine. The strong and vivid thought entered his mind, "What if I should find the resident in a pool of blood." He did not even slow his walk as he banished the thought from his mind. At this point, he could not see the resident's door. He continued, and as he passed the door, he noticed it was slightly ajar and the light was on. His conscious thought as he passed was, "Gosh, he must have stayed up all night worrying." He retraced his path to the door to say "Hello", opened the door, and found that the bed was covered with a large pool of blood and the resident dead.

Thus two doctors were aware, unconsciously, of the exact method that was to be used in the suicide (bleeding to death), but neither had conscious thoughts even of the possibility of suicide.

Second case

A young female college student was started in psychotherapy following a serious depression. Her family history was very poor. Her mother was a paranoid schizophrenic. Her father committed suicide when the patient was two. A young uncle hung himself in a house across the street from the patient's home when the patient was in her teens.

After a stormy 18 months of therapy which had been marked by several periods of suicidal preoccupation and threats, the patient witnessed a successful suicide by a woman who jumped under the wheels of a subway train (the same method used by the father to kill himself). This experience made the patient

"feel better", but at the same time it was clear evidence that suicide was a way out.

She had separated herself from her psychotic mother and was doing well socially when she was suddenly faced with a mass of emotional trauma. First, the frequency of her visits had been reduced, due to realistic reasons, by the therapist. Second, an armed man of another race forced his way into her apartment and almost choked her to death in a rape attempt before being frightened off. Third, coincidentally, her mother was hospitalized for a recurrence of her psychosis, and the family stated, "If you had stayed at home, this wouldn't have happened." Fourth, she was faced with economic and social problems. Her main ego support, her successful work at college, was threatened by all of these events.

She came to the treatment hour with a razor in her pocket. Because she was so disturbed, the therapist offered her an additional hour if she would wait while the next scheduled patient was being seen. She accepted, but during the hour locked herself in the office powder room and at 7:20 p.m. slashed her wrists, losing about a pint of blood from superficial veins. When she was found by the therapist, her cuts were treated, and she had a satisfactory therapy hour following this event.

Upon her return home, her best friend, a young female art student, called her by phone to ask, "What happened at seven tonight? I had the strangest feeling and drew a picture of it." The patient asked the artist to bring the painting to her, and she, in turn, brought it to her therapist. The artist had been seated in her living room, reading a magazine, when the impulse caused her to draw the picture. The artist is clinically normal, has no overt symptoms, and no particular knowledge of psychiatry.

The picture portrays an upraised, tense, transparent human hand against a multicolored background of blotches of vivid color through which irregular thin lines run. The wrist is cut, and there is brilliant red blood flowing freely from the cut. A number of tiny human figures are drawn as climbing upon the hand. The artist stated that as she drew the picture "the hand represented a human being (the patient) wanting to commit suicide." The little figures "mock the human being for taking life so seriously, instead of accepting it." The thin lines represent "life as a puzzle or broken as glass."

There had been no communication of any ordinary kind between the two girls for two weeks preceding the drawing of the hand. Neither the patient, her therapist, nor the artist could have known previously that the patient would have an appointment on the day and at the hour she did. Her appointments were irregular and scheduled only a week in advance.

Previous suicide threats had never included cutting, but were limited to jumping in front of a train or barbiturate overdosage.

Discussion

When we seek explanations for unusual phenomena, the simple possibilities should be considered first. Among these are 1) simple coincidence, 2) fraud for gain, 3) the notorious unreliability of witnesses, and 4) the distortion of memory by the passage of time.

Case 1 is understandable if it is assumed that there is non-verbal and non-conscious communication of emotional feeling between individuals. This is reasonably accepted.

It is difficult to account for the phenomena on the basis of coincidence, especially in case 2, since the artist had not drawn violence before or after the single water color described. The most striking point is the knowledge of the exact moment the suicidal action took place, as well as the method.

The reliability of the information in both cases is felt to be very good.

It is difficult to visualize much in the way of "secondary gain" for the people involved. The fact that the events were reported within a very short time of their occurrence should help minimize the effects of distortion of memory.

These cases are presented with the hope that they will stimulate further study in respect to the method in which such strong, clear and vivid impressions are communicated from one person to another.

49 Copley Road
Upper Darby, Pennsylvania

CONTRIBUTIONS OF THE RORSCHACH TEST TO THE UNDERSTANDING OF "ACTING-OUT" BEHAVIOR

JOSEPH M. SACKS[1] AND MURRAY L. COHEN[2]

A number of papers have been written in an atheoretical manner concerned with the use of the Rorschach in discriminating between acting-out behavior and normal behavior. The results have been largely in a positive direction. The present paper is addressed to the theoretical meaningfulness of the Rorschach and its clinical usefulness, not only as a tool for differential diagnosis but also as an instrument which can give us a better understanding of the structural and dynamic aspects of acting-out behavior.

Our point of view is that a broader perspective can be achieved in examining the Rorschach records of cases of character disorder with acting-out features by bearing in mind the relationships between certain concepts underlying Rorschach scoring and the processes of ego development.

Rorschach (4) noted empirically that individuals who gave several responses to the blots involving human figures in motion (M responses) tended to be stable, reflective and empathic, while those who responded to the blots largely in terms of color (C responses) tended to be unstable, impulsive and egocentric. He suggested that the ratio of the number of Movement to the number of Color responses (M:C) would represent the balance between these two sets of tendencies within the individual. Recent attempts to validate these hypotheses experimentally have yielded results in essential agreement with them (5, 7). Rorschach also observed that pedantic individuals who suppress or inhibit both fantasy activity and emotional responsivity responded to the blots almost completely in terms of their form. He concluded that the combination of accurate form with movement would indicate the extent to which fantasy is controlled, while the combination of accurate form with color would indicate the extent to which affect is controlled. The use of shading, i.e., the nuances of black and gray in the blots, is considered by later investigators (3) to represent a sensitivity to the emergence into awareness of unacceptable affect or fantasy and the consequent mobilization of defenses, with accompanying anxiety. Again, the form-accuracy of the responses reflects the effectiveness of such defensive operations.

The content of Rorschach responses offers clues to fantasies which are related to personality structure and dynamics in terms of sources of anxiety, direction of hostility, psychosexual level, basic passivity, and dependency conflicts (2, 6).

Rorschach's concept of the Movement:Color ratio was represented in terms of an introversion-extratension continuum. There is also a marked relationship between this concept and Freud's description of ego development. In his paper, "Formulations regarding the two principles in mental functioning", Freud (1) postulates that in the infant a disturbance in the state of mental equilibrium by the demands of needs which are not immediately satisfied leads to an hallucinatory experience of the need gratifying object and to diffuse motor activity. This pattern represents a primitive attempt at satisfaction and is abandoned since it fails to provide gratification. Substituted for the hallucinatory experience, over the course of time, is the perception of reality, i.e., differentiation of what is true from what is not true. This is conceptualized as the development of the reality ego from the pleasure ego. The next step is the coordination of the primitive diffuse motor discharge into activity appropriate to the alteration of reality, in terms of action aimed at need gratification. In order that the action should be appropriate, restraint becomes necessary so that the action will observe the limits imposed by reality. Such restraint is achieved through the process of goal-directed thinking which is a covert, experimental way of acting with a minimal, but not negligible, discharge of impulses. Thus, goal-directed thinking makes it possible to

[1] Chief, Clinical Psychology Service, VA Hospital, Brockton, Mass.
[2] Department of Psychology, Boston University.

contain tension when reality requires the delay of motor discharge. Freud points out that the substitution of the pleasure ego by reality ego does not eliminate the pleasure principle, but actually safeguards it by giving up immediate and uncertain pleasures for assured future pleasures. Another mode of thought activity which helps to accomplish restraint (while still remaining under the dominance of the pleasure principle) is fantasy. This is more primitive than goal-directed thinking and closer to hallucinations which are its prototype. Uncontrolled, this is autism. When it is utilized deliberately by imaginative and creative individuals, we might refer to this mode of thought as fantasy in the service of the ego.

Obviously aberrations can and do take place in various phases of this development; e.g., in surrender to fantasy, in obsessive thinking which paralyzes action, in uncontrolled motor discharge, or in all sorts of combinations of these. We can deduce from Freud's formulations that so-called "acting-out" behavior represents an aberrant or incomplete development of the ego: tension is not contained by the process of thought; motor discharge cannot be delayed; action is aimed at immediate gratification of desires; and ability to differentiate the true from the untrue is impaired. Since acting-out individuals do not have the capacity for adequate fantasy in the service of the ego, they possess little ability to project into the future. Thus there is no means available to them for judging the consequences of behavior.

It is precisely this information, i.e., tension contained by thought, delay of impulse discharge, etc., which the Rorschach offers. On the basis of these relationships between Rorschach concepts and the processes of ego development, we feel that the test has great value with respect to diagnosis, prognosis and treatment planning of individuals described as "acting-out" or impulse characters. The Rorschach can provide information as to the context of the lack of control and to the individual's potentialities for development of control. There will be good prognosis with findings of anxiety related to the acting-out, the presence of fantasy activity and capacity for empathy, judgment and planning. Conversely, a poor prognosis will be present with findings of a dominance of uncontrolled affect with minimal anxiety, little empathy, poor judgment, and a lack of capacity for reflective, planful thinking.

The following case study illustrates many of the relationships discussed above between personality structure and the Rorschach record as they are manifested in the clinical history.

Robert was first seen in the Criminally Insane Building of a State Hospital on the East Coast. He was awaiting removal to a penitentiary to serve a 15-year sentence on a conviction of assault with intent to commit carnal abuse. This was his only civil conviction. While in the service, however, he had been charged but not convicted of rape and inciting a riot. During his hospitalization he was assaultive at the least provocation; he was an elopement risk and was kept under constant surveillance.

When seen, Robert was 20 years old. He was the second of two children, having a sister two years older. His father was a successful engineer in the midwest who found it necessary to be away from home for long periods of time. The patient stated that the father did not get along well with the other members of the family, but the patient himself describes the father as kind and sincere although he could not get close to him. The patient sees his mother as a very sweet and sympathetic person who was oversentimental. A casework report states that the relationship between Robert and his mother was never a good one. They quarreled a great deal, and on a number of occasions he struck her. She was never able to manage him.

There is very little else known about the patient's early life. He completed nine years of schooling and then left school with a history of truancy and disobedience of the school authorities.

No unusual sexual experiences were disclosed. The patient himself stated that he learned where babies come from when he was 7 or 8 and that he had his first heterosexual experience at age 13.

Physically, the patient was 5′ 5″ tall and weighed about 155 pounds. He was extremely fair complexioned, and had blue eyes and blond hair which fell slightly over the right side of his forehead. His facial expression was generally friendly and almost guileless, completely belying his frequent hostile outbursts.

The psychiatric description of the patient highlights the absence of restraint and his lack of judgment. He was described as moody, temperamental, easily irritated, arrogant, unstable, assaultive and homicidal. The psychiatric evaluation stated that Robert was an impulse neurotic with aggressive behavior "as an attempt to compensate for feelings of inferiority and inadequacy." For this conclusion the psychiatrist referred to a phobia of the patient for "big things". The patient stated that he felt small next to big things and was frightened of them.

Rorschach interpretation. The tendency towards impulsive hebavior is quite apparent in the M:C ratio of 1:7.5. Further indication of a lack of control

is the finding that less than 50% of his color responses were form dominated. Responses to the ink blots determined solely by form represent only 22% of his total responses and reflect a relative lack of intellectual control. They also indicate that his judgment of the external world is excessively influenced by inner needs. This influence does not lead to distortion (he does not have any poor form responses: F + % is equal to 100%), but it is apparent that his relationships with others have a large narcissistic element.

Analysis of the content points to a major conflict between dependency and independency. The passive quality is reflected in the content categories of plants, household items, clothing and nature. The independent-assertive aspect is seen in the responses of fire, explosion, and the extensor activity in his one movement response. Such responses as "falling petals", "a burning spire" and particularly "a skeleton dancing over a fire" corroborate the clinical impression that the patient's behavior is associated with a compensation for inadequacy feelings.

A number of factors are present, however, which indicate the presence of positive assets and a potentially favorable prognosis. Robert gave four responses determined by the shading qualities of the ink blots. These reflect the presence of anxiety which we presume to be related to his lack of control. Further, in spite of the marked imbalance between M and the sum C, there is at least one abortive M response. Also, he was able to give four color responses in which the form was dominant. Thus, the patient has at least a minimal potentiality to form emphatic relationships and to direct to some degree the free discharge of impulses; he does have fantasy available for the control of discharge. On the basis of these findings we can assume that the pathological behavior seen in the clinical history might be influenced by the intervention of a therapeutic relationship. Despite the pathological behavior seen in the clinical history, we feel that Robert has potentialities for response to a psychotherapeutic relationship if this could be offered.

Too often psychologists using the Rorschach with acting-out characters have been prone to elaborate the negative aspects of the case. In the discussion presented an affirmative and positive approach is developed. The concordance of test concepts and the concepts of psychoanalytic theory can be utilized with respect to positive aspects, prognosis and treatment planning. The following record is presented for illustrative purposes and was selected to highlight our point of view.

Rorschach Protocol and Scoring

Card I. 1. Looks like a bat. It looks like those could be wings and these could be the feet. 2. Looks like some sort of insect, maybe a tarantula. The shape of it and the black spots on its back.

1. W F+ A P; 2. W FY+ A

Card II. 1. This doesn't look like anything as a whole, but part of it looks like a burning building. This looks like a spire in a picture of Morocco. (Burning?) The red looks like it's in the shape of a flame. 2. (V) This part looks like a bomb explosion. A bomb bursting, the red portion looks like flame and its lines directed upward could be pieces of shrapnel.

1. Dd FC+ Fi; 2. D CF+ Ex, Fi

Card III. 1. This looks like a skeleton. The head of it looks like a skull and he is dancing. 2. Dancing over a fire. The color of it gives the impression of fire. 3. (V) Upside down it looks like it could be a vase. A child's sketch of a vase in water color.

1. D M+ (H) P; 2. D C Fi; 3. Dd FC+ Hh

Card IV. 1. This looks like a buffalo hide, shape of the legs and head and not the color, but it seems to have texture or sheen the way a pelt would have.

1. W FT+ A P

Card V. 1. This looks like it might be the shadow of a butterfly. It looks like the outline, that gives the impression because it's black.

1. W FY+ A P

Card VI. 1. This looks like an Indian head dress. These could be feathers and this is the piece that sticks in front of the head. 2. And an animal hide. It seems to have a sheen to it like a pelt, like it has texture.

1. D F+ Cg; C FT+ A P

Card VII. 1. This looks like a colored woman. Siamese twins joined together here. The color indicates they are not white.

1. W FY+ H P

Card VIII. 1. This looks like a flower. They call them elephant ears. It is the color and these could be falling petals, the leaves and the stem.

1. W CF+ Pl

Card IX. 1. (V) This looks like a mushroom cloud of the atomic bomb. This looks like an

explosion. These are gases given off and flames and this is the vacuum created. It is oval shaped and shaped like a mushroom. 2. This way it looks like a flower. This looks like a flower, petals, leaves and it's colored that way.

1. W FC+ Ex, Fi; 2. W FC+ Pl

Card X. 1. This looks like something you might see in an aquarium. 2. It looks like coral, coral because of the colors and shapes. 3. And these might represent crabs.

1. W CF+ N; 2. C CF+ N; 3. D F+ A P

Summary

R	= 18	M	= 1	H	= 1
P	= 7	FT	= 2	(H)	= 1
W	= 9	FY	= 3	A	= 6
D	= 7	FC	= 4	Fi	= 2 + 2
Dd	= 2	CF	= 4	Ex	= 2
		C	= 1	Cg	= 1
		F+	= 3	Hh	= 1
				N	= 1
				Pl	= 2

BIBLIOGRAPHY

1. Freud, S.: *Collected Papers*, Vol. IV. London: The Hogarth Press, 1948.
2. Hammer, E. F., and Jacks, I.: Study of Rorschach flexor and extensor movement. *J. Clin. Psychol., 11:* 63–67, 1955.
3. Klopfer, B., *et al.*: *Developments in the Rorschach Technique.* Yonkers-on-Hudson, N. Y.: World Book Co., 1954.
4. Rorschach, H.: *Psychodiagnostics,* New York: Grune & Stratton, 1942.
5. Rosenthal, M.: Some behavioral correlates of the Rorschach experience-balance. Unpublished doctoral dissertation, Boston University, 1954.
6. Schafer, Roy: *Psychoanalytic Interpretation in Rorschach Testing.* New York: Grune & Stratton, 1954.
7. Singer, J. L., and Herman, J.: Motor and fantasy correlates of Rorschach human movement responses. *J. Consult. Psychol., 18:* 325–331, 1954.

AN APPROACH TO THE TREATMENT OF THE METABOLO-PSYCHIC COMPONENT OF CERTAIN EUTHYROID STATES

A Preliminary Report

NATHAN MASOR, M.D.[1]

Introduction

Thyroid and its derivatives have been used for many years in the treatment of lowered metabolic states such as myxedema and cretinism. It has also been used in euthyroid states such as sterility, habitual abortion, obesity of pituitary origin, eczemas and in some allergies. More recently, it has been thought to be effective in adjusting the lipoid metabolism in diseases such as atherosclerosis, the lipoid stages of cirrhosis of the liver, etc.

There have been many reports in recent months on the use of 3-5-3 L-triiodothyronine in patients with metabolic insufficiency. This condition is characterized by lethargy, emotional instability, dullness, apathy, lowered basal metabolic rate, with a normal serum protein-bound iodine, normal radioactive uptake and normal cholesterol values. Such patients, it has been shown, respond poorly to desiccated thyroid, but receive excellent relief from 3-5-3-L triiodothyronine (1).

However, it has been noted by certain investigators that adjustment of the metabolic factor in atherosclerosis with an oral thyroid extract mixture was accompanied by a marked concomitant improvement in the metabolo-psychic component of the atherosclerotic diseases. It therefore occurred to this observer that patients without organic disease who suffered from a moderate or severe anxiety state might likewise experience improvement, especially since this treatment had been shown to be harmless in the many hundreds of serious organic cases treated by the investigators (2, 3).

Selection of Patients

A large series of patients, who upon complete physical examination were found to be organically sound and who, in addition, were subjected to extensive laboratory and x-ray examinations, including G.I. series, gall bladder series, I.V.P., basal metabolism P.B.I., serum cholesterol, complete blood count and sedimentation rate, were selected for treatment. The diagnoses in these cases included anxiety states, severe and moderate; constitutional psychopathic states; migraine; "psychogenic" rheumatism; and obesity of endogenous and/or exogenous origin.

The study also included a number of patients suffering from the clinical entity of hypometabolism wherein the only abnormal variant from the above group was the subnormal basal metabolism.

Principle of Treatment

The same approach as was used by the investigators in adjusting the lipoid metabolism for atherosclerotic states was used in the clinical cases to be described. The most important principle underlying the administration of thyroid hormone is the very *gradual* increase in its level from week to week and from month to month.

The second important principle is that of administering simultaneously vitamin factors which aid the general intracellular oxidative metabolic processes (4). The recognition of these two principles is of paramount importance in reaching an optimum maintenance dosage level of circulating thyroid to create sustained symptomatic improvement. It has been found that the side reactions which are present when thyroid is administered alone (tachycardia, palpitation, nervousness, insomnia, etc.) are virtually eliminated if the above principles are kept in mind.

Therapy

A. Diet. All of the patients in therapy were given high protein low cholesterol diet and lowered caloric intake wherever indicated (5).

B. Specific therapy. Patients were cautioned to eliminate all palliative measures which

[1] Associate Attending Physician, Parkway Hospital, New York City.

were being used to control their symptoms. These included chlorpromazine, ataractic drugs, sedatives, hormones, barbiturates, etc. The following substances were used: 1) Oxytropin,[2] 2) Lipotropin,[3] 3) Co-Thyro-Bal.[4] These patients had all previously been treated with non-specific multi-vitamin therapy, including parenteral B-12, with inconsequential results.

Case Reports

Case 1: N. F., female, married, no children, age 33. Chief complaints insomnia, severe upper abdominal pain, tenseness, irritability, depression, asthenia, anorexia. She was sure that she had an internal cancer and that there was no hope for her because of the prolonged (seven-year) unsuccessful treatment by many physicians, including the author. She was subjected to complete diagnostic survey prior to therapy, without pathological findings. Previous therapeutic measures, including psychotherapy, during the seven years had proved of no value, adding to her feeling of futility and creating a sense of impending catastrophe. She was placed on Oxytropin T 10 and given an injection of Co-Thyro-Bal intravenously. The dose of Oxytropin was increased to T 12 within two weeks, and later further increased to T 15. She was given an injection of Co-Thyro-Bal intravenously, which was repeated each week. By the end of the third week amelioration of all the above symptoms had occurred, and at time of writing she had a feeling of stability and well-being not previously experienced. Besides her own feeling of well-being, her husband has confirmed this drastic change in her comportment.

Case 2: R. F., 58, female, married, owner of candy store. Chief complaints: severe melancholia, manifested by constant depression, weeping, forgetfulness, inability to concentrate, exhaustion and magnification of her domestic problems, with paranoid trends. Had undergone complete psychiatric processing, including shock Rx, and use of ataractic drugs—with only transient partial amelioration of her mental state. After Oxytropin T 10, Lipotropin and Co-Thyro-Bal intravenously had been given, there was an almost euphoric reversal which lasted about two weeks. After about a week the patient had a recurrence of symptoms, though milder in extent. Raising the Oxytropin level produced a marked improvement so that the patient had been satisfied to stay on the oral therapy almost exclusively and would come in for her injection at infrequent intervals. Her dose level at the present time is Oxytropin T 20.

Case 3: M. K., male, age 46. History of migraine for many years, requiring absence from work. He was a very tense individual, reacting with extreme emotion to stress. Prompt, sustained relief was obtained with the above therapy, without recourse to other medicaments. An accompanying incidental arthropody, previously considered to be of psychogenic origin (since no confirmatory evidence of organic joint disease was discovered), concurrently disappeared during treatment with Oxytropin, Co-Thyro-Bal, Lipotropin.

Case 4: M. K., female, single, age 56. An individual seemingly well adjusted to her environment and superior in intellect, who occupies a responsible position. On the job she had an extreme inner tension. Irritability, moodiness and exhaustion, which was not manifested outwardly while working, would become strongly evidenced when at home. She had for a period of years used sedatives and later ataractic drugs, with no benefit. The patient took very little time to adjust to low dosage Oxytropin and Co-Thyro-Bal, and as a result feels and acts much more relaxed. Most noteworthy in her case is the fact that tiredness, irritability and insomnia are rarely present now.

Case 5: M. F., age 41, height 5′5½″, weight 265. She had gained 70 pounds in the previous eighteen months. Her main complaint was not the evident obesity but the marked emotional instability (apprehension, hyperactivity, restlessness, etc.) which would be slightly relieved by frequent excursions to the refrigerator. She had no apparent personal or domestic problems that could account for her anxiety. The obesity was considered exogenous since laboratory findings were negative. Oxytropin and Co-Thyro-Bal caused such a calming effect within a few weeks that she was able to abstain from her overeating and has begun to lose weight satisfactorily.

The Evaluation of Therapy

It is difficult to evaluate the results of treatment in patients who presented no pathological or positive clinical findings to start with. Therefore, subjective comfort is the only yardstick for measuring results. Previous experience with these types of patients, using placebo therapy, has only resulted in the patient's looking for relief elsewhere. None of the usual controls is possible in such ambulatory patients, especially since they are often acutely disturbed and more than anything else are seeking immediate relief. The patients' previous inability to improve with the usual palliative types of therapy must be the base line from which to evaluate the therapeutic response with thyroid-vitamin therapy.

No attempt has been made to form a

[2] Oxytropin: Each oral tablet contains thyroid extract in varying dosages (10 mg. to 60 mg.) combined with vitamin factors in constant amounts; thiamin chloride, 20 mg.; riboflavin, 10 mg.; niacinamide, 120 mg.,; ascorbic acid, 100 mg.

[3] Lipotropin: Each oral tablet contains: choline, 422 mg.; pyridoxine hydrochloride, 2 mg.; inositol, 134 mg.

[4] Co-Thyro-Bal: Equal parts of sodium levo-thyroxin and crystalline B-12 in a lyophilized mixture for parenteral use.

statistical survey in terms of absolute relief because of the difficulty in measuring metabolo-psychic complaints quantitatively. It takes from six weeks to six months to create a stabilized adjustment of the metabolism, and this paper is a preliminary report based on numerous observations only. Sufficient time must elapse before results can be compiled statistically.

Discussion

The original investigators intended the above-mentioned therapy for use primarily in atherosclerosis (2, 3). They were interested in halting organic vascular changes and in delaying cholesterol and lipoid deposition. The euphoric aspect of the treatment and its relief in chronic fatigue states prompted the writer to investigational study in euthyroid states such as those described. When used according to the principles enumerated, no real toxicity or side effects had been noted, other than an occasional mild temporary tremulousness at the very start of therapy. Moreover, the institution of such therapy in euthyroid states will not raise the basal metabolic rate but will lower significantly hypercholesterolemia.

There is considerable variation in the time it takes for patients to obtain relief and the length of time that such relief prevails, so that the adjustment of dosage and intervals of injections of Co-Thyro-Bal become an individual specific problem in each case. There has long been a fear of giving thyroid derivatives to the thin, anxious, nervous, mentally distressed person. On the contrary, if the principles enumerated above are followed, such a person will actually gain weight and become more relaxed. On the other hand, obese individuals when kept on optimum therapeutic dosage levels and low caloric intake will lose weight.

Summary

A method has been described wherein gradually increasing doses of desiccated thyroid in fixed combination with the oxytropic factors of the B-complex plus ascorbic acid (orally) and levo-thyroxin in combination with B-12 (parenterally) exert an euphoric and calming effect on the metabolo-psychic component present in certain euthyroid states. Using this method there have been virtually none of the side reactions which usually occur when extract thyroid is used alone.

BIBLIOGRAPHY

1. Tittle, C. R.: Effects of 3-5-3 L-triiodothyronine in patients with metabolic insufficiency. *J. A. M. A. 162*: 271–274, 1956.
2. Israel, M.: An effective therapeutic approach to the control of atherosclerosis illustrating harmlessness of prolonged use of thyroid hormone in coronary disease. *Am. J. Digest. Dis., 22:* 161–168, 1955.
3. Bamford, T. E., Jr.: Treatment of neurologic and psychiatric disorders secondary to arteriosclerosis: A preliminary report. *New York J. Med., 51:* 2913, 1951.
4. Heuper, W. C.: Prevention and treatment of atherosclerosis. *M. Clin. North America, 33:* 773, 1949.
5. Morrison, L. M.: Arteriosclerosis, Recent advances in dietary and medicinal treatment. *J. A. M. A., 145:* 1232–1236, 1951.

392 Forest Avenue
Staten Island 1, New York

PREMATURE WAKING AND POST-DORMITIAL PARALYSIS[1]

MAX LEVIN, M.D.

Sleep paralysis may be pre-dormitial or post-dormitial, depending on whether it precedes or follows sleep. In post-dormitial paralysis the patient wakes up paralyzed for a fraction of a minute, being unable to make any movement but breathe; the paralysis ends abruptly.

Sleep paralysis occurs in normal people but seems to be especially common in narcolepsy. It may assume special forms, as in diplopia (1) and paralysis of memory (2).

Sleep paralysis is a manifestation of asynchrony in the flow and ebb of inhibition. Flow (irradiation) of inhibition over the brain eventually produces sleep. Ebb of inhibition (disinhibition) produces waking. Though the highest motor centers are part of the "substrate of consciousness" (3), we must make an artificial distinction and speak of them as two separate things. As sleep overtakes us, inhibition is irradiating over the brain. Ordinarily the highest motor centers do not succumb to inhibition until the substrate of consciousness succumbs. This may be inferred from the fact that we are able to move as long as we still awake (though, to be sure, in the last moments the "will to move" falls off more or less). Conversely, when we wake up we are able to move the moment we open our eyes, showing that disinhibition of the highest motor centers accompanies that of the substrate of consciousness. As regards the flow and ebb of inhibition the highest motor centers and the substrate of consciousness march side by side. This timing is disturbed in sleep paralysis. In pre-dormitial paralysis inhibition has overtaken motor centers while the substrate of consciousness is still excitable (we are still awake). Conversely, in post-dormitial paralysis inhibition has been lifted from the substrate of consciousness while motor centers are lagging behind, still under its spell.

The object of this paper is to raise the question, Can a stimulus that wakes the sleeper before his proper time conduce to post-dormitial paralysis?

We wake in one of two ways. Either we "sleep ourselves out" and wake spontaneously, or we are wakened prematurely by some stimulus such as an alarm clock. Even when we wake from an alarm clock, we are usually able to move when we open our eyes. This shows that disinhibition is usually simultaneous in motor centers and substrate of consciousness, even when waking is premature. But sometimes the waking stimulus seems to catch the motor centers before they are "slept out", before they are ready for action. The clearest example is one from my own experience.

Case Report

I was born in 1901. Though I do not have narcolepsy, I have for some years (perhaps 15 or 20) had attacks of post-dormitial paralysis, occurring several times a year. In the attack I know I am in bed but am otherwise not aware of my surroundings. My eyes are closed. I am conscious of complete inability to move, except to breathe. Breathing seems to be labored, so that I have the idea (during the attack) that the blanket is over my mouth, but can do nothing about it. There is extreme discomfort and anxiety. Though I have been interested in sleep paralysis for years and was the first to employ this phrase in the title of an article (4), never yet has the thought flashed through my mind, "This is only an attack of sleep paralysis; I must have patience; it will soon pass." I seem to hope that relief will come with the next breath, but each breath leaves me still paralyzed. Finally, after half a dozen unsuccessful attempts, on the next breath I feel as if I am making a Herculean effort, and immediately the spell is broken and I am wide awake and in full possession of my faculties.

The incident that gave rise to this paper was the following: I woke and became aware of numbness and tingling in my entire right upper limb. I knew I was in bed and knew

[1] From the Department of Neurology and Neurosurgery, The New York Medical College, Flower and Fifth Avenue Hospitals, New York, New York.

my arm was hanging over the edge of the bed in such a way that the mattress was pressed against the armpit. Otherwise I was not aware of my surroundings. The numbness and tingling were progressive and very uncomfortable. I tried to move my arm and could not. I realized I could make no movement other than breathe. Uppermost in my mind was the idea that I was developing a "plexus palsy", a phrase that was sharp in my consciousness. I lay thinking, "Here I am, with my arm over the edge of the bed. If I don't soon move my arm I will wind up with a plexus palsy. If only I could move my arm!" I did not know I was having an attack. I was conscious of slow labored breathing. I took it for granted that if there was any possibility of moving my arm it would be during inspiration. With each breath I tried to move it and failed. After each breath it seemed like an eternity till the next one, when I would try again. The mood was one of black despair. Six or eight breaths passed fruitlessly. Finally on the next breath there was the Herculean effort, with instant relief. Wide awake, I now saw that my arm had indeed been hanging over the edge of the bed.

It is tempting to think that stimuli from pressure on axillary structures had partially awakened me before my motor centers had been "slept out". It seems fair to suppose, or at any rate to suspect, that when people are wakened prematurely, there will now and then be instances when motor centers are caught "unprepared", not yet ready for duty.

It is noteworthy that in all my attacks there is a feeling that motor potentiality is associated with inspiration, and each attack ends with an inspiration accompanied by a Herculean effort that seems to "burst the chains" that had confined me. In paralysis that is total except for breathing, potentiality for movement is at a minimum, and what little there is may be expected to exist at the moment of taking a breath. Like the spark that ignites a gasoline mixture, the excitation that occurs at this moment disinhibits the rest of the motor apparatus (when at last it is ready for disinhibition).

BIBLIOGRAPHY

1. Levin, M.: Diplopia in narcolepsy, *Arch. Ophth. 28:* 942–957, 1943.
2. Levin, M.: Thinking disturbances in delirium. *Arch. Neurol. & Psychiat., 75:* 62–66, 1956.
3. Levin, M.: Reflex action in the highest cerebral centers: a tribute to Hughlings Jackson. *J. Nerv. & Ment. Dis., 118:* 481–493, 1953.
4. Levin, M.: The pathogenesis of narcolepsy, with a consideration of sleep-paralysis and localized sleep. *J. Neurol. & Psychopath., 14:* 1–14, 1933.

350 Central Park West
New York 25, N. Y.

SOCIETY PROCEEDINGS

NEW YORK NEUROLOGICAL SOCIETY AND THE NEW YORK ACADEMY OF MEDICINE, SECTION ON NEUROLOGY AND PSYCHIATRY

Joint Meeting, October 9, 1956

Abner Wolf, M.D., President, New York Neurological Society, presiding

PRESIDENTIAL ADDRESS: PRENATAL INFECTIONS OF THE CENTRAL NERVOUS SYSTEM. DR. ABNER WOLF.

PRESUMED ROLE OF GLIAL CELLS. DR. SAUL KOREY.

A significant concentration of glial cells from white matter of the brains of lambs has been achieved by means of differential sedimentation. The cells are partially damaged since the mechanical means of separating them from the substance of the white matter necessarily cuts the processes of the glial cells. In addition the hyperosmolarity of the media used causes extraction of both water and water-soluble constituents from the cells to some extent. Within these limitations the procedure achieves the isolation of about 10 per cent of available glial cells in the white matter with a purification of about 15 times. The nucleotide, lipids, and protein constituents of the cells were discussed as means of reference for further work. The cells respire with a QO_2 of about 5.

Discussion—DR. ABNER WOLF: Dr. Korey has given us a very stimulating revue of investigations of the role of neuroglia in the central nervous system. He has presented the fruits of his first attempts to isolate glial cells, and we all hope with him, that this will open the path to further investigation of their functions. The first great wave of interest in, and accumulation of data on the neuroglia, was that of the famous German school of neuropathologists, active at the turn of the century and just before it. The Spanish school of neuroanatomists then made further historic contribution to our store of knowledge in this field. Now, the American and English schools of neuroanatomy, neuropathology and biochemistry are attacking the problem. Dr. Korey is one of those who promises to contribute greatly.

Dr. Zimmerman, may I call on you for discussion?

DR. HARRY M. ZIMMERMAN: I don't know why Dr. Wolf calls on me, as a morphologist, except in retribution for Dr. Korey's essay in the field of morphology, and I presume he wants me to talk about biochemistry! Actually, some years ago we tried some of the work which Dr. Korey did and were a little discouraged from the morphologic standpoint. We were not certain how much cytoplasm those cells really contained. Moreover, we were a little worried as to whether the damage produced by saturated sucrose interfered with metabolic processes sufficiently to prevent accurate analyses of the kind described by Dr. Korey. So that, unless we analyzed purely for lipids and proteins, in other words, the dead constituents of the cell, the results would be meaningless. We did not think vital biochemistry could be done, and so we abandoned the field to someone who is much more able than we are, and we will wait the two years for Dr. Korey to come back and tell us what this all means. Much of what he has told us has to do with the proof that these cells still have cytoplasm, and I would like to know, what of it?

DR. FRITZ CRAMER: In contrasting this method with morphologic studies and tissue cultures, it was inferred that no true references can be drawn from them as to "respiration". Are these cells or these cultures living, and are you therefore drawing inferences as to respiration on the part of functioning, living cells? I did not get that point.

DR. SAUL KOREY: In answer to Dr. Cramer, these are cells that are harvested from the white matter which we obtained by removing by suction all the overlying gray matter. Then we have the strips of white matter; we homogenize this in a particular way and centrifuge it. After that we keep filtering it through various screens until we get to a point where we can centrifuge the suspension in a density gradient; after we centrifuge at 18,000g the myelin fragments in this medium rise to the surface and the cells are left at a lower interface. We are able to remove the cells after we remove the myelin.

When the cell respires, this is sufficient to start with. I would say the carbonic anhydrase is very high in white matter, for example. At this particular moment we are in a position to see if it is a glial component. There are two problems: one is what we study, whether it is a synthetic group or a hydrolytic group of enzymes. If we start with acetate and are building up long chain molecules or cyclical compounds there is a synthetic group of enzymes involved. If we are studying enzymes that cleave an ester down into an acid and alcohol, then these enzymes which are hydrolytic are easier to retain and examine in such a preparation. Carbonic anhydrase, which is a "simple" system, may be preserved in our preparation. The second problem is whether what we observe relates back to the tissues *in situ*. There is no simple answer to that.

EXPERIMENTAL CRYPTOCOCCOSIS (TORULOSIS). DR. SEYMOUR LEVINE.

Experimental cryptococcosis was produced by subcutaneous, intracerebral and intraperitoneal inoculations using three strains of *C. neoformans*. The subcutaneous lesions were characterized by early leuko-

cytic response, abscess formation, encapsulation, healing, and only occasional instances of dissemination. Brain lesions were characterized by proliferation of the yeast cells to form large lesions with little inflammation and with universal dissemination. More inflammation was noted in the meninges, but here, too, the reaction was weak and irregular. Intraperitoneal inoculations were attended by an intermediate degree of inflammatory response (usually most marked in the liver), and were also intermediate with respect to dissemination and lethality. The predilection for the brain in cases of dissemination was thought to be directly related to the paucity of inflammatory response in cerebral tissue.

The presence of healing subcutaneous cryptococcal abscesses failed to confer active immunity against subsequent intracerebral challenge.

The inflammatory response to subcutaneous inoculation of *C. neoformans* was abolished by cortisone, and, to a lesser extent, by x-radiation. This was accompanied by a marked increase in dissemination.

Discussion—Dr. Harry M. Zimmerman: The question I asked Dr. Korey of course I asked Dr. Levine in my own laboratory, and the reason why these experiments were undertaken Dr. Levine has already told you. We were not interested in infecting a group of mice with an organism which is uncommon in this part of the world to see the results in rodents; we were more interested in what to do about these almost universally fatal cases of cryptococcosis we see in man. In the past ten or twelve years we have had ten cases, and we were convinced that the fatal outcome had something to do with a lack of tissue response to the infecting organism. It was for this reason that Dr. Levine undertook to isolate the polysaccharides from the organism in cultures, and for weeks and months my laboratory was jammed with flasks in which he was growing them in order to get capsular material. He did not tell you that many mice were injected with the capsular material without any immunity being produced in the animals, and this, in order to find out why capsular material would not produce immunity, led him to the experimental results which he presented. I cannot elaborate on them, because I think Dr. Levine has adequately done so.

Dr. Saul Korey: I should like to ask Dr. Levine whether he feels this reactive difference in cerebral tissue, where the vascular tissue contains enough leukocytes even compared to the skin, is an immunologic difference, or is it due to the fact that there is a lot of cortisone-like material around in the brain to prevent the reactive response, or does he feel there is an immune difference in the actual leukocytic series in the brain?

Dr. Seymour Levine: I wish I could answer that question. It is obviously the question that I have been asking myself every time I studied the slides. I noticed in my sections that when leukocytes did appear in the brain they were often in relation to the choroid plexus or the meninges, and I wonder if there is not a quantitative difference in the amount of blood supply or the number of connective tissue cells that are available in the brain, or perhaps in some other factor in a quantitative sense rather than a qualitative sense. That is the only possible answer I can offer.

NEW YORK NEUROLOGICAL SOCIETY AND THE NEW YORK ACADEMY OF MEDICINE, SECTION ON NEUROLOGY AND PSYCHIATRY

Joint Meeting, December 11, 1956

Rollo J. Masselink, M.D., Secretary, New York Neurological Society, presiding

The Organic Mental Syndromes: Elementary Consideration. Dr. Samuel Thomas.

A definition is given for the organic mental syndrome. Productive and reductive symptoms are distinguished, and exemplified in disturbances of perception, attention, awareness, orientation, memory, behavior, personal habits, judgement, conduct as a whole, content and sequence of thinking, character, individuality. Symptoms of certain special conditions are assigned their places in this list. Further psychological factors are mentioned briefly. The reductive symptoms are considered more characteristic of the organic mental syndromes than the productive.

Discussion—Dr. Thomas K. Davis: I should like first to commend Dr. Thomas for giving such a good paper. I am critical of the title—not a serious criticism indeed.

If we use elementary, as it sometimes is used, to imply incompleteness and the mere rudiments of a topic, his titeling does disservice to his production. No doubt he is using elementary in the more exact sense—as that which deals with the elements of a subject.

I think Dr. Thomas has demonstrated tonight that he is a neuropsychiatrist who writes a paper from what he has observed and not from what he has read. His is to my mind an original approach. Another thing which I would like to commend is his excellent choice of adjectives as he goes along to define the various elements.

Incidentally, one notes the happy absence of psychiatric clichés.

Cases of Calcification and Ossification of the Spinal Leptomeninges with Myelopathy and Radiculopathy. Dr. Fritz Cramer and Dr. James Correll.

Whereas small calcifications in the leptomeninges are met frequently and are of no clinical significance, this report describes seven cases with massive calcifications in which there was undoubted clinical significance. Despite calcific masses one or two centimeters by sev-

eral centimeters long and several millimeters thick, they were not revealed by x-rays. On lumbar puncture a manometric block was often present but spinal fluid protein was low. Myelograms revealed atypical defects or a block.

The neurologic symptoms corresponded to the location of the calcifications, *i.e.*, they were myelitic or radicular, in type.

The etiology of the calcifications or ossifications was probably diverse. Among probable causes were direct trauma in one case; bacterial meningitis in one case; and, in another case three spinal anesthesias in close sequence, each with sequelae. The only other finding of possible etiologic significance, present in the majority of cases, was the presence of degenerative osteoarthropathies. In two cases there was early calcification of a thoracic intervertebral disc.

Two types of calcified and ossified leptomeningeal thickening were seen. In one type the ossification occurred over the spinal cord, while in the other type nerve roots were compromised. The neurologic symptoms corresponded to the location of the calcification, *i.e.*, were myelitic or radicular in type. The calcific masses in themselves are capable of producing symptoms by virtue of their space-taking nature. They probably cause both direct pressure upon the new structures involved and also compromise them secondarily by impairing local vascular circulation.

In these cases surgical exploration should be carried out. When the lesions involve the nerve roots improvement follows, but when the spinal cord is affected the results are less encouraging.

Discussion—Dr. Jack London: I should like to ask how thick those plaques were, and where does the bone come from? What was the origin of the bone you talked about?

Dr. Samuel Federman: Were any of your cases diagnosed pre-operatively?

Dr. Rollo J. Masselink: I should like to ask if on review of the x-rays after the diagnosis was established, were you able to pick up the calcification that was missed pre-operatively.

Dr. Fritz Cramer: Dr. Wolf was going to discuss the matter of the origin of the calcification, and, in his absence, I will undertake to discuss it as I understand it from the literature. Most of the reports on this condition are of French and German origin, and interestingly enough, they ascribe the primary meningeal reaction and subsequent calcification as due mostly to syphilis, and particularly, tabes. Other conditions where one finds some thickening of the arachnoid, sometimes with calcification, are long-standing disturbances of the neuraxis with secondary degeneration, the heredodegenerative diseases, and syringomyelia; also in any localized inflammation, arthropathy, including diseases of the intervertebral discs, and tumefaction outside the dura. I think that we are dealing here in our cases with a group of perhaps different etiologies, but it is of interest that we should have had one case in which previous direct trauma in the area was undoubtedly an etiologic factor in causing calcification, and that we found no syphilis and no reaction to syphilis in any of our cases. Those patients in whom the spinal cord was involved probably had a different etiology from those in whom the arachnoid was involved near the nerve roots.

The most appealing explanation I have come across from the German and French literature is that the calcification is located dorsally because of the compartmentation, so to speak, of the arachnoid space. Posteriorly in the midline is the so-called ligamentum posticum of Schwalbe, connecting the pia and arachnoid. Then out laterally are the normal webs between the arachnoid and the pia, connecting them with the spinal cord, dentate ligament, nerve roots and blood vessels. In certain instances, let us say the intramedullary diseases of the spinal cord, there are abnormal products of the metabolism, and the catabolism of the cord, and these are of a different nature from the normal protein within the spinal subarachnoid space. In the case of spinal cord tumor causing a block and stagnation and increased protein, the protein is virtually pure plasma, exuding from tortuous veins. We do not find massive adhesions; we may find some adhesions and flecks of calcium, but adhesive processes are not the typical picture. In the adhesive conditions we do not find an increased protein. In them, it may well be that products of degenerescence arising within the diseased spinal cord cause an irritation of the leptomeninges which then results in thickening and eventually in calcification.

Now to come to the questions which I may not have answered: 1) the thickness of the plaques was 1 to 2 to 5 millimeters. 2) the bone is simply the end-stage in the laying down of calcium in the thickened arachnoid. 3) a preoperative diagnosis of calcification was not made in any of our cases. The one which was quoted in the German literature of recent origin in which they showed two roentgenograms and a pathologic specimen revealed the calcification beautifully.

Dr. Masselink: In looking back over the x-rays, could you see the calcification?

Dr. Cramer: In looking back over the x-rays in our personal cases there may be some faint signs of the calcification, but they are not sufficiently convincing to make the diagnosis possible.

The Dependence on Narcotic Drugs. Sandor Rado, M.D., D. Pol. Sc.

To achieve clarity, we have separated the pathology of drug dependence from the pathology of the underlying disorder, applying to both the insights of adaptational psychodynamics. In this light, drug dependence is seen to be a self-inflicted process of miscarried repair; it transforms realistic self-government into narcotic self-government. Utilizing our previously suggested concepts of narcotic pleasure-effect, narcotic elation and narcotic craving, we have shown that both elation and craving are interdependent manifestations of a narcotic delusion of grandeur elicited by and anchored in the pleasure effect of the drug. This delusion is explained by the bribing action effortless pleasure has on the system of hedonic self-regulation, which forces the organism to repeat this type of pleasure again and again. From this malignant pathology we deduced the plan for rehabilitation: withdrawal of the drug; reconstructive psychoanalytic therapy whose goal is to con-

trol the potential dangers of suicide and relapse, and, whenever feasible, to eradicate the underlying disorder. Finally, attention was called to the need to advance the physiology of pleasure which may well hold the key to the patient's biochemical immunization against the intoxicating pleasure-effect of narcotic drugs.

Discussion—Dr. Daniel M. Shapiro: Dr. Rado's contribution tonight illuminates a challenging problem, the *specific* effects of narcotics on the motivational structures of the addict, and the unique significance it has in his life.

Ten years ago when I was a resident at the Hospital for Narcotic Addict Treatment at Lexington, I first became familiar with Dr. Rado's early brilliant efforts to penetrate the maze of addiction. Tonight's reformulations in terms of adaptational theory are clear and penetrating; they should advance our solution of the knotty problem of the treatment of the addicted person.

BOOK NOTES AND REVIEWS

Books received are acknowledged and given a brief description in this section. Selections serving a variety of interests will be made from these for a more extensive review, as far as space will allow.

BOOK NOTES

Gesell, Arnold, Ilg, Frances L. and Ames, Louise Bates: YOUTH—THE YEARS FROM TEN TO SIXTEEN. [New York: Harper and Brothers, 1956. Pp. 542. $5.95.]

The senior author of this book, Dr. Arnold Gesell, has been an outstanding student of child development for many years. He founded the Clinic of Child Development at Yale University in 1911 and directed it for 37 years during which a great deal of sound research on child development and behavior was published by himself and associates.

The present book is the third volume of a series of studies. The first entitled "Infant and Child in the Culture of Today", was published in 1943, and the second was "The Child from Five to Ten" appearing in 1946. These two books had a profound influence in the fields of pediatrics and psychiatry and also many of the findings were utilized by educators and others associated with child development.

The present text is presented in three parts, the first of which is for the purpose of orientation and to explain the basic concepts. The second part offers a complete account of adolescent traits, thinking and overt behavior during the seven year period and the third part gives a perspective of the sequences of growth for nine principal areas of behavior development. These areas are total action system, self care and routines, emotions, the growing self, interpersonal relationships, activities and interests, school life, ethical sense and philosophic outlook. Over a span of twelve years there were 550 contacts with 115 children in the "Care Group" plus 50 more seen at only one age.

This remarkable study by highly trained and experienced observers furnishes a wealth of information for anyone engaged in the problems and course of development of the growing adolescent.

Freud, Sigmund: THE INTERPRETATION OF DREAMS. Translated from the German and Edited by James Strachey. [New York: Basic Books, Inc., 1955. Pp. 692. $7.50.]

This famous book has been available in German (Die Traumdentung) to mental specialists since 1900 and in English since 1913 when it was translated by the late A. A. Brill. The present translation is the most satisfactory one and is also enhanced by a much needed editorial illumination of points not clearly understood by others. The work is considerably enhanced by explanatory footnotes and bibliographies.

In this book Freud made one of his most (if not, in fact, his most) original contributions explaining the workings of the unconscious, and for some time his fame rested largely on its contents. It is very valuable after these many years as a historical volume in the development and understanding of psychoanalysis. This new translation should be in every library of members of the psychiatric profession.

Hess, W. R.: HYPOTHALAMUS UND THALAMUS. [Stuttgart: Georg Thieme, 1956. Pp. 70, 246 illustration. D. M. 36.]

This beautifully illustrated atlas constitutes Part III of studies of the brain stem which are the result of experimental work initiated by Prof. Hess in 1924 and continued for nearly 30 years and for which he received the Nobel Prize. The volume consists of photographs showing sections of the brain stem of cats at various levels with sites of stimulation, and pictures of the reactions with a verbal description of the behavior of the animals. A unique and valuable feature is the English translation of the entire German text in parallel columns.

The technique developed by Professor Hess

consists of inserting electrodes in the living cat which allows stimulation at will during its normal life-behavior. Thus by appropriate stimulation of the hypothalamic and thalamic regions many simple and complex autonomic responses, as well as the motor behavior that accompanies them can be produced. It is a most valuable document for all concerned with neurophysiology and neuroanatomy illustrating the application of a remarkable research technique.

Kretschmer, Ernst: MEDIZINISCHE PSYCHOLOGIE (Eleventh Edition). [Stuttgart: Georg Thieme, 1956. Pp. 382. Illustrated. D.M. 29.60.]

This edition of the well-known German textbook has been revised and enlarged to include up to date findings and ideas in the field of medical psychology. The book was first published some 35 years ago at which time it presented fresh new thoughts and concepts, a practice that has characterized subsequent editions.

Many additions to the present volume represent work carried out or directed by the author himself, but the experimental investigations of Lorenz and Tinbergen are presented as well as a new chapter on projective tests written with C. Schick. The subjects of constitutional physiology of development and correlations between body-build and autonomic regulations are interestingly discussed as is also the analysis of psychomotor activity.

It is doubtful if any other book on medical psychology today contains the variety of sound, useful information that is to be found in this contribution to mental science. The author obviously has a unique orientation in this large field.

White, R. W.: THE ABNORMAL PERSONALITY (Second Edition). [New York: The Ronald Press, 1956. Pp. 644. $6.50.]

This book is a well organized and presented text on the organization, integration and disintegration of the personality. Its extensive use for beginners has justified this second edition which has been revised thoroughly to bring in the most recent research contributions, to introduce more therapeutic aspects and to include more concepts of prevention of personality disorders.

Instructors in psychology and psychiatry will do well to recommend this book to students of courses in abnormal psychology since it not only covers the subject well but is written in an easily understood, yet scientific, style with adequate documentation and useful indexes.

Laughlin, Henry P.: THE NEUROSES IN CLINICAL PRACTICE. [Philadelphia and London: W. B. Saunders Company, 1956. Pp. 802. $12.50.]

The author of this comprehensive book presents the various problems of the neuroses and their manifold ramifications as he has "encountered them in clinical practice". It contains an abundance of material bearing on diagnosis, symptoms, psychodynamic mechanisms and therapy. The chapter summaries and references are useful features.

The text is well organized in that it begins with the universal reaction of anxiety and ends with a chapter on the neuroses following trauma. All of the classical neuroses and some of the oddities of "normal" individuals are included in special topics.

Enhancing its value as a reference book are thirty two tables, two hundred sixteen illustrative case summaries, an appendix giving an outline classification of mental illnesses, an extensive glossary of psychiatric concepts and terms, an index of personal names and one of subjects. This book covers its subject in a way that will be of interest and value to psychiatric practitioners and of particular usefulness to students and teachers of psychiatry in the medical schools.

English, O. Spurgean and Finch, Stuart: INTRODUCTION TO PSYCHIATRY. [New York, 1954. W. W. Norton & Co. $7.00.]

The authors have attempted to introduce a psychiatric text which is not only comprehensive but designed for the beginner in Psychiatry. In addition, to the usual histories. Doctor's English and Finch have added a succinct dynamic description of the various diagnostic categories. Freud's formulations are utilized to explain the development of the "normal" and the pathological.

The first part of the book describes personality formation through the successive stages of libido and ego development, yet in terminology

which is free of the obscurities of analytic jargon. Pathological character formations and its metapsychological implications are lucidly described. There are separate chapters on neurotic disorders, psychophysiological reactions, psychotic disorders, organic brain syndromes and mental deficiency.

The text has minor defects which are due to the attempts of the authors to cover the entire area of psychiatry; *e.g.*, child psychiatry is covered in a cursory fashion. The author's bibliography mentions all the important works, yet in the actual text, no reference is made to other workers whose formulations may not concur with the authors. The book contains a wealth of material and should be required reading for psychiatrists, psychologists, and social workers.

BOOK REVIEW

Bash, K. W. LEHRBUCH DER ALLGEMEINEN PSYCHOPATHOLOGIE. GRUNDBEGRIFFE UND KLINIK. With a preface by H. Binder and a contribution by H. Landolt. [Stuttgart: Georg Thieme Verlag. 1955. Pp. XII+288, 10 illustrations. 50 case histories. D.M. 29.50.]

To add another textbook of psychopathology to the existent stock is a daring undertaking which this volume fully justifies. Its background is the European clinical tradition of phenomenal description. Based on this tradition the author conceives and arranges the psychopathological material in an original fashion which beyond mere eclecticism intricately utilizes the spade work in psychological research of the past half century.

The approach thus gained receives its theoretical support from physiologic, biologic, depthpsychologic and gestaltpsychologic sources, incorporating a great deal of factual information including work done in the Western hemisphere. This broad synoptic view necessarily trespasses the self-imposed limitations of the various schools of thought. Nevertheless, the author is unmistakably Jungian in his orientation. (He is a member of the Board of the C. G. Jung Institute, Zürich.) Mention shall be made of the excellent clinical presentation in Part III of the book, which deals with Jung's four basic 'typological' functions: sensation, feeling, intuition and thinking. In the preceding parts the author's theory of the "unstructured psychic qualities" *Bewusstheit-Unbewusstheit* (conscious awareness or unawareness) as against the psychic "regions" (in the topological sense of the word) of *das Bewusste-das Unbewusste* (the conscious-the unconscious) are discussed and contrasted to the meaning of *Bewusstsein-Unbewusstsein*. The latter pair of terms is elsewhere rendered by the author as conscious or unconscious mind and the word "mind" is used ". . . to suggest the commonly accepted systemic character of the psychic regions so designated, the fact that they exhibit respectively a kind of typical, albeit as yet undefinable organization and coherence." In Part II the psychological concepts of field and gestalt structure are elaborated upon and enlarged to include such terms as archetype and complex. The remainder of the book is given to the description of symptoms and syndromes. Here one finds in addition to discussion of the usual disturbances (the mnesias, orientation, the organic syndrome, etc.) such up-to-date topics as the general adaptation syndrome, the focal interference syndrome of M. Bleuler and W. C. Halstead, and finally the syndrome of gestalt decay.

H. WALLER

BOOKS RECEIVED FOR REVIEW

DECEMBER, 1956

NACHT, S. La Psychanalyse d'Aujourd'hui. Presses Universitaires de France, Paris, France.

VAN RIPER, CHARLES AND GRUBER, LESLIE. A Case-book in Stuttering. Harper & Brothers, New York, New York.

WALTON, JOHN N. Subarachnoid Haemorrhage. The Williams & Wilkins Co., Baltimore, Maryland.

NOTES AND NEWS

V.A. PROJECT ON MULTIPLE SCLEROSIS

Multiple sclerosis, one of the "mystery" diseases of medicine, is under investigation in collaborative research just begun by the Veterans Administration, the National Research Council, and the National Institute of Neurological Diseases and Blindness, of the National Institutes of Health.

The project is aimed at finding what role, if any, is played in the development and progress of the disease by geographic, climatic, and allied environmental factors.

The collaborative study will concern itself with members of the armed forces and veterans who have developed the disease during and since World War II.

The doctors participating in the project are particularly interested in learning in what latitudes, climates, and geographic areas these people have lived.

Since multiple sclerosis is more prevalent in the northern United States and Canada than in the south, an effort will be made to determine if veterans contracting the disease have benefited if and when they have moved to warmer climates.

The investigation will involve the study of medical and other official military and VA records of the men afflicted by multiple sclerosis.

In addition to seeking to assess the major environmental factors to which these men have been exposed, the investigators also will study data concerning physical characteristics and defects noted during induction, the degree of stress involved in the performance of military duties, race, occupation, and medical history of parents and other relatives.

Dr. Benedict Nagler, chief of the neurology division of VA central office in Washington, D. C., is principal investigator.

Dr. Nagler's associates in the project are Dr. L. T. Kurland, chief of the epidemiology branch, National Institute of Neurological Diseases and Blindness, National Institutes of Health; Dr. Gilbert W. Beebe, statistician of the division of medical sciences, National Research Council, National Academy of Sciences; Dr. J. F. Kurtzke, chief of the neurological service of the VA hospital in Coatesville, Pa., and Dr. Eugene L. Youngue, chief of the neurological service of the Leech Farm Road VA hospital in Pittsburgh, Pa.

There have been about 2,000 cases of multiple sclerosis among men in the armed forces between 1942 and the present, and an even greater number among veterans after discharge.

The investigators expect to have available for study the records of 1,000 cases in the armed forces and of more than 2,000 cases involving veterans. Most of the military records will come from Army World War II files in St. Louis.

TRANS-CULTURAL STUDIES IN PSYCHIATRY

After considerable planning over the last several years a section on trans-cultural studies in psychiatry has been set up in the Department of Psychiatry at McGill University. The working co-operation of psychiatrists in 18 countries has been obtained and projects are being put into operation. The first of these was jointly set up by the Department of Psychiatry and the Department of Sociology and Anthropology of McGill University and was initiated last year at Lima, Peru in association with the Department of Psychiatry of the Hospital Obrero under the leadership of Dr. Alberto Seguin. This project deals with the relative significance of psychological, socio-cultural and physiological factors in the etiology of the psychosomatic disorders arising from the movement of Highland Indians to coastal cities.

A second project which has been launched is the compiling of a newsletter based upon information sent in from our various co-workers in other countries. This material has been assembled and is now being sent out to psychiatrists in other countries interested in trans-cultural studies in psychiatry. Those wishing to obtain copies should write to Dr. E. D. Wittkower, Section on Trans-Cultural

Studies, Allan Memorial Institute, 1025 Pine Avenue West, Montreal, P. Quebec.

NORTH SHORE HEALTH RESORT SERIES

The ninth lecture in the Seventh Annual North Shore Health Resort Lecture Series on "The Medical Practitioner's Contributions Toward Healthy Emotional Development (The Physician as a Counselor)" will be held at our hospital, 225 Sheridan Road in Winnetka, Illinois on Wednesday, June 5, 1957 at 8:00 p.m. "Problems of Grandparents" will be discussed by Erich Lindemann, M.D., Professor of Psychiatry, Harvard Medical School; Psychiatrist-in-Chief, Massachusetts General Hospital; Director, Human Relations Service of Wellesley, Inc.

INTERNATIONAL PSYCHOANALYTIC ASSOCIATION

The 20th International Congress of Psychoanalysis, organized by the Société Psychanalytique de Paris will be held July 28–August 1, 1957 in Paris. *President:* Dr. Heinz Hartmann, President of the International Psychoanalytic Association. *Programme Committee:* Dr. Edward Kronold, 17 East 96th Street, New York 28, N. Y., U. S. A. *Organisation Committee:* Dr. S. Nacht, 187, rue Saint-Jacques, Paris 5º, France.

PANELS FOR INTERNATIONAL CONGRESS

The Programm Committee wishes to announce the formation of the following Panels for the 20th Congress of the International Psychoanalytic Association in Paris, July 28–August 1, 1957: 1) *Contributions of Direct Child Observation to Psychoanalysis*—Moderator: Dr. Ernst Kris Main presentation: Miss Anna Freud Members of the Panel: Dr. E. C. M. Frijling-Schreuder, Dr. Liselotte Frankl, Mrs. Melanie Klein, Dr. Marianne Kris, Dr. René A. Spitz, Dr. D. W. Winnicott; 2) *Neurotic Ego Distortions*—Moderator: Dr. Robert Waelder Main presentation: Dr. Maxwell Gitelson Members of the Panel: Dr. W. H. Gillespie, Dr. Edward Glover, Dr. Maurits Katan, Dr. Sacha Nacht; 3) *Variations in Technique*—Moderator: Dr. Ralph R. Greenson Main presentation: Dr. Rudolph Loewenstein Members of the Panel: Dr. Maurice Bouvet, Dr. K. R. Eissler, Dr. Sylvia Payne, Dr. Annie Reich.